TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA

A THESIS SUBMITTED TO

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT (PUNJAB)

IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF

DOCTOR OF MEDICINE

IN

MEDICINE

2023

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Dedicated

to

my Family

&

Teachers

ACKNOWLEDGEMENT

I am highly thankful and grateful to the Almighty for making me able to write and complete my thesis. I take this opportunity to express my gratitude to everyone who has been part of this journey. I sincerely thank my mentor Dr.H.S.Dhooria, Associate professor in Department of General Medicine DMC&H, Ludhiana, under whose excellent guidance I have completed my thesis. His able and mature approach, ever willing help made the task simpler. He has always been patient and kind to me.

I would like to thank my co-supervisor Dr. Dinesh Gupta, Professor and the Head of the department, General Medicine who has always lent me a helping hand. His valuable suggestions and scholarly guidance is highly appreciated. I acknowledge the guidance of my co supervisor Dr. Davinder Paul, Associate Professor and the Head of the department, Medical oncology who has always motivated me to do better. This was a great learning opportunity for me to learn from my mentors who have always been an epitome of excellence for me.

Words are not enough to thank my parents Mr Tilak Mehta and Mrs Pinki, my sister Dr. Girisha Bassi and my brother in law Dr Sagar Bassi for believing in me, for supporting me and always motivating me to do better. They have always inspired me and have been my strength throughout this journey. Heartfelt thanks to my friends and colleagues, Dr Rishav, Dr. Gautam, Dr. Deepshikha and Dr.Shivika for being available all the time and making these times less stressful. A sincere thanks to my juniors Dr. Kajal, Dr.Vansh and Dr.Amandeep for helping me whenever needed.

Thanks to all my patients who have been part of this study and DMC&H staff and residents who made this task possible. Special and inexpressible thanks to Mrs Namita and Mr.Naveen, Research and Development Center for their efforts and contribution.

Dr Akshay Mehta

ABBREVIATIONS

A/G ratio: albumin/ globulin ratio

ALP: alkaline phosphatase

ASR: Age Standardized Rate

BMM: bone marrow microenvironment

CRAB: calcium, renal impairment, anemia, and bone lesions

CT/PET: computed tomography/positron emission tomography

DAMA: Discharge against medical advise

DMCH: Dayanand Medical College and Hospital

EMD: extramedullary disease

ESR: Erythrocyte sedimentation rate

FDG: fluorodeoxyglucose

FGF3: fibroblast growth factor 3

FISH: Fluorescence in situ hybridization

FLC: free light chain

HB: hemoglobin

i.e: that is

IQR: interquartile range

ISS: International Staging System

LDH: lactate dehydrogenase

MGUS: monoclonal gammopathy of undetermined significance

MM: Multiple Myeloma

MRI: magnetic resonance imaging

NDMM: newly diagnosed Multiple Myeloma

OPG: osteoprotegrin

OS: overall survival

PET-CT: Positron emission tomograpgy- computed tomography

PFS: progression free survival

POEMS: polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes

RANKL: receptor activator of NFκB ligand

RDW: red cell distribution width

SMM: Smoldering multiple myeloma

SREs: skeletal-related events

TLC: Total leucocyte count

TTP: time to progression

ABSTRACT

Introduction - Multiple myeloma (MM) is a disorder caused by neoplastic proliferation of a clone of malignant plasma cells. Typical clinical features are generalised weakness, fatigue, bone pain, anemia, renal insufficiency and hypercalcemia. Incidental discovery on comprehensive laboratory panels is common. Serum or urine protein electrophoresis or immunofixation and bone marrow aspirate analysis helps in diagnosis of multiple myeloma. Various clinical and laboratory parameters have been established for the diagnosis of MM.

Aim of Study: 1) To study the clinical profile in newly diagnosed cases of Multiple Myeloma. 2) To study the molecular profile in newly diagnosed cases of Multiple Myeloma..

Materials & Methods: The study was conducted in the Department of Medicine, Department of Oncology and the Allied Specialties of Medicine of DMCH, Ludhiana. 62 newly diagnosed cases of multiple myeloma diagnosed between 1st March 2021 and 28th Feb 2022 were included in the study from both indoor and outdoor departments of the hospital. Physical examination, radiological investigations and routine laboratory investigations, bone marrow examination, serum protein electrophoresis and molecular profile were recorded. Patients were staged according to revised international staging system (R-ISS) and correlation between molecular profile and various parameters was studied.

Results: In this study, among 62 patients, 36 were males and 26 were females. The mean age was 61.6±8.5 years. The common complaints were fatigue, weakness and bone pain. Hb<10gm/dl was seen in 46 patients. Serum creatinine >2gm/dl was seen in 41 patients. Corrected calcium >11mg/dl was seen in 53 patients and serum β2 micro globulin >5.5mg/l was seen in 34 patients. ESR was raised in all patients. Lytic lesions were the most common radiological finding in the study seen in 37 patients. M-spike was seen in 58 patients. 33 patients out of 62 had positive molecular profile- out of which 13 patients had t(11:14), 10 patients had t(4:14), 7 patients had t(14:16) and 3 patients had p53 del. As per R-ISS staging, 28 patients presented in stage II and 34 in stage III while no patient presented with stage I disease.

Conclusion: This study showed that multiple myeloma is a disease of middle and elderly aged population with male preponderance, with male female ratio of 1.4:1. Various parameters like age, male to female ratio, clinical presentation, serum creatinine, serum beta 2 microglobulin, serum LDH and molecular profile were comparable to the other studies. However, a higher percentage of patients had hypercalcemia, anemia and majority of patients presented in stage III in our study.

Keywords: Multiple Myeloma, Molecular profile, R-ISS

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INTRODUCTION

Background of the Study

Multiple Myeloma (plasma cell myeloma, plasmacytic myeloma, myelotomies, Kahler's disease) represents a malignant proliferation of plasma cells derived from B cell[1]. It is more commonly seen in farmers, wood workers and leather workers. Incidence of MM is lowest in Asian countries than African American and European countries but it is increasing rapidly[2]. According to 2017 data, the Age Standardised Rate for MM incidence in India is 0.7/1 lakh population amounting to about 6800 new cases a year. It's median age of diagnosis is 52-61 years but is less common under 40 years. Male are affected more than females.[3]

Diagnostic criteria for Multiple Myeloma:

1) Clonal bone marrow plasma cells or biopsy proven bony or extramedullary plasmacytoma and any one of the following myeloma defining events.

2) Evidence of one or more end organ damage that can be attributed to the underlying plasma cell proliferative disorder specifically:
   - Hypercalcemia: serum calcium > 0.25mmol/l (>1 mg/dl) higher than the upper limit of normal or > 2.75mmol/l (>11mg/dl).
   - Renal insufficiency: creatinine clearance 177micromol/l (>2 mg/dl)
   - Anemia: hemoglobin value of >2.0gm/dl below the lower limit of normal or hemoglobin value <10.0 gm/dl
   - Bone lesions: one or more osteolytic lesions on skeletal radiography, CT or PET CT
   - Any one or more of the following biomarkers of malignancy:
     - Clonal bone marrow plasma cells percentage ≥60 %
     - Involved: uninvolved serum free light chain ratio ≥100
     - >1 focal lesions on MRI studies[2]

It causes multiorgan dysfunction and symptoms such as renal failure, bony pains or fracture, anemia, susceptibility to infections, hypercalcemia, neurologic symptoms and manifestation of hyper viscosity. It is more commonly seen in farmers, wood workers and leather workers[2]. It is characterized by the development of osteolytic lesion in the bone and involves the activation of osteoclasts with simultaneous suppression of new bone formation by osteoblast inhibition[4]. Bone pain is the most common symptom. Other presentation is anemia, hypercalcemia, renal failure and weight loss. Rare features are cord compression, CNS involvement[5]. Immunomodulatory agents like thalidomide, lenalidomide and protease inhibitor like bortezomib along with dexamethasone is a good induction therapy and has good response rate. Autologous stem cell transplant is good option in selected patients after induction therapy[6]. This study aims at clinical profile of newly diagnosed multiple myeloma patients in India.

Multiple Myeloma

Myeloma is a blood cancer of cells found in the bone marrow, specifically the so-called “plasma cells.” The bone marrow is a spongy tissue inside the bones that normally creates different parts of the blood. Plasma cells are a key part of the body's immune system. They produce antibodies that help the body fight infection. Myeloma begins when healthy plasma cells change and grow out of control. This may result in multiple bone lesions that increase the risk of bone fractures. That is where the phrase "multiple myeloma" comes from.[7]

Malignant proliferation of plasma cells derived from a single clone is termed as Multiple Myeloma. The Plasma cell dyscrasia is broad heading which include this type of diseases. Multiple myeloma is the second most common hematological malignancy after Non-Hodgkin’s Lymphoma and it accounts for 15% of all hematological malignancies. The incidence of this disease increases with age in a spectrum of 4/lakh in the general population to around 30/lakh in over 25 years population. Even though lots

of advancements have been made in the pathogenesis and etiology of this disease, it has still not made its way into the category of curable diseases.[7]

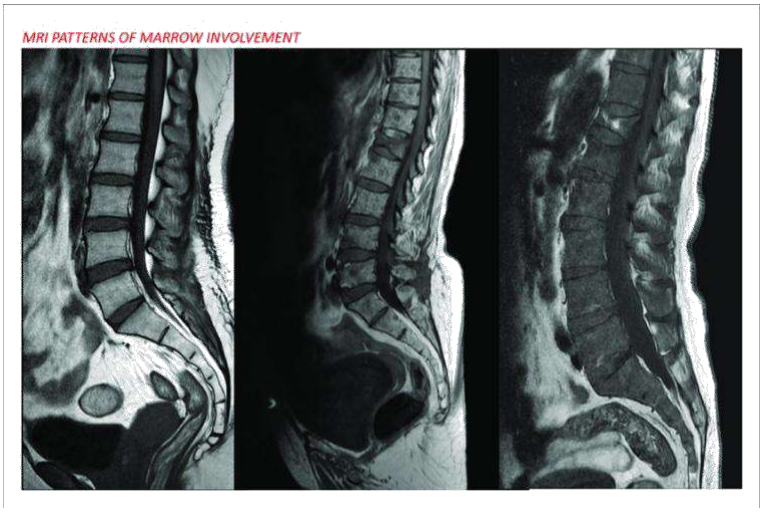

Figure 1: Normal Bone marrow ((left) and Multiple Myeloma (right)

Egyptian mummies showered light to describe diseases which were similar to Multiple Myeloma. In 1844, Samuel Solley reported a case of myeloma in Sarah Newbury. He described it as “mollitis ossium”. Together with Bence Jones; he found that the urine analysis of the patient showed a protein with the heat properties often observed for urinary light chains. It later on came to be known as the Bence Jones Protein. MacIntyre and Dalrymple described the properties of the affected bone in the same patient and MacIntyre called it Mollitis and Fragillis ossium.[8,9]

As per the GLOBOCAN/IARC data, the worldwide Age Standardized Rate (ASR) for incidence of MM is 1.4/1,00,000 population accounts to 1,00,000 new cases every year. In the US as per the SEER data, the ASR for incidence is higher at 5.8/1,00,000 population accounting for 21,000 new cases each year. Worldwide the 5 year prevalence of the disease is 2, 10, 697 or 4.3/1, 00,000 population. The ASR for MM incidence in India is 0.7/1, 00,000 population amounting to about 6,800 new cases a year.[10]

Present clinical research focuses on the balance between treatment efficacy and quality of life, the optimum sequencing of treatment options, the question of long-term remission and potential cure by multimodal treatment, the pre-emptive treatment of high-risk smoldering myeloma, and the role of maintenance. Upcoming results of ongoing clinical trials, together with a pipeline of promising new treatments, raise the hope for continuous improvements in the prognosis of patients with myeloma in the future.[11] The introduction of high-dose melphalan with autologous stem cell transplantation and the availability of molecular targeted novel agents such as immune-modulatory drugs and proteasome inhibitors have dramatically changed the treatment strategies for MM. Achievement of a high response rate resulted in the extension of overall survival, but further research and the development of more multimodality therapeutic approaches is warranted to cure this disease. [12]

The reclassification of a subset of patients with smoldering MM, based on high-risk biomarkers, and the development of the revised international staging system are among the key new developments in diagnosis and staging.[13] Compared with MM patients diagnosed in earlier years, those diagnosed after 2010 had higher rates of novel therapy use and better survival outcomes. Patients diagnosed in 2012 were 1.25 times more likely to survive 2 years than those diagnosed in 2006.[14]

Multiple myeloma is a malignant disorder characterized by proliferation of a single clone of plasma cells derived from the beta cells in the bone marrow. It is the second most common adult hematological malignancy and it is the most common cancer with skeletal components as its primary site. Multiple myeloma is a neoplastic plasma cell dyscrasia characterized by a clinical pentad:

a) anemia
b) monoclonal protein in serum or urine or both
c) abnormal bone radiographs and bone pain
d) hypercalcemia and renal insufficiency or failure.

With the exception of monoclonal gammopathy of undetermined significance, it is the most common plasma cell dyscrasia, with an incidence of approximately 4.5/1, 00,000 per year in the United States. Incidence increases with age [median age of diagnosis is around 69 years], is almost equal in males and in females and higher among blacks than in whites. [15] The exact cause of multiple myeloma is unknown. Increased incidence has been reported in people exposed to radiation[16], petroleum, rubber, wood and plaster products, cosmetologists and farmers. Viruses may also be involved in the pathogenesis. Genetic aberrations have been noted in 20-60% patients with t(11:14) being the most frequent translocation. Among the losses, monosomy or partial deletion of chromosome 13 is the most common finding[17]. A variety of chromosomal alterations have been found in patients with myeloma: hyper diploidy, 13q14 deletions, translocations t (11:14), t (14:16), t (4:14), 1q amplification or 1p deletion, deletion 17p13. However no single common molecular pathogenetic pathway has yet emerged. Molecular Profile includes the myeloma panel workup which includes the translocations – t (11:14), t (14:16), t (4:14) and deletion - del 17p13 (p53). Cytokines play an important role in the proliferation of myeloma cells. The growth and differentiation of myeloma cells is supported by interleukin-6.

The clinical manifestations are due to the infiltration by plasma cells and secretion of the monoclonal protein M by them. Replacement of the marrow by plasma cells and renal damage produces anemia which may present as pallor, fatigue etc. Hemoglobin concentration of less than 12.0 gm/dl occurs in 40-73% of patients at presentation and contributes to weakness and fatigue in as much as 82% of patients. The anemia is normochromic, normocytic in most patients. Bone pain is the predominant symptom in 80% patients. An increase in osteoclastic bone resorption in myeloma is usually associated with a marked impairment in bone formation. Approximately 75% of patients had punched out lytic lesions, osteoporosis or fractures on conventional radiography[18]. Nerve root

compression may occur due to vertebral collapse. Hypercalcemia occurs in 18-30% patients as a result of bone destruction. Approximately 13% had concentrations greater than 11mg/dl. The patient with hypercalcemia may complain of fatigue, constipation, nausea or confusion.[18]

Patients of multiple myeloma are at risk for developing recurrent infections due to deficiency in antibody production; abnormal cell mediated immunity, and in advanced cases, neutropenia. Approximately 25% of myeloma patients have a serum creatinine value greater than 2mg/dl at diagnosis[19].Various factors may contribute to renal failure, including cast nephropathy, hypercalcemia, dehydration, hyperuricemia and the use of nephrotoxic drugs. A hyperviscosity syndrome may occur leading to headaches and visual disturbances.[19]

The spectrum of neurological complications in multiple myeloma ranges from direct compression, radiculopathy, spinal cord compression, peripheral neuropathy, slowed mentation from hyper viscosity, hypercalcemia or uremia, autoimmune or cytokine mediated peripheral neuropathy. Rarely, POEMS syndrome[1] (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) observed in osteosclerotic myeloma with prominent sensory neuropathy.[1]

NEED FOR THE STUDY

Multiple myeloma (MM) is a disorder caused by neoplastic proliferation of a clone of malignant plasma cells. The incidence of myeloma is highest in African-American and Pacific islanders, intermediate in Europeans and North Americans and lowest in developing countries including Asia. The incidence of multiple myeloma (MM) is increasing rapidly in Asian countries. MM will eventually become a tremendous medical burden in this region, challenging the health-care systems of Asian countries. Because of huge disparities in economy, lack of adequate health-care

infrastructure and the lack of access to novel drugs in our country, treatment of MM is still a challenge to medical field in India. In India, the estimated incidence according to Globocan 2012 is 6,955 new cases, mortality of 6,027- and 5-years prevalence estimate of 11,886[6].

MM comprises 13% of hematologic malignancies. The characteristic features of MM include accumulation of monoclonal plasma cells in the bone marrow associated with monoclonal immunoglobulin (Ig) synthesis and osteolytic bone lesions. The clinical features of the illness usually include bone pain, which is also a common presentation of other disease conditions in this peculiar age group. Complications such as renal failure, infections, anemia, lytic bone lesions and amyloidosis lead to morbidity as well as mortality[20]. Though most patients of MM are symptomatic at presentation needing prompt treatment, about 10-15% may remain asymptomatic in whom treatment may be delayed. This leads to delay in diagnosis as well as mis referrals, which usually in the long run affect treatment outcome. A high index of suspicion by the physician is therefore important and may be guided by the knowledge of common presenting clinical symptoms. Evaluation of the common investigations, presenting features, especially in a resource poor and predominantly local population will serve as a guide and necessary aid to early diagnosis[21].

Raised calcium, renal impairment, anemia, and bone lesions (CRAB) are the currently accepted diagnostic criteria for diagnosis of symptomatic (and therefore treatable) myeloma. Although magnetic resonance imaging (MRI) and computed tomography/positron emission tomography (CT/PET) are very sensitive and may provide more information in certain cases, limited facilities as well as finances have limited the use of these diagnostic tools in resource poor settings where simple X-ray of bone is still considered as a standard investigation. Prognostic markers such as β_2 microglobulin may not be easily assayed in some parts of the country or affordable by some patients. However, to the unsuspecting physician, these investigations are not usually regarded as baseline and the

diagnosis is usually delayed till complications begin to occur. It may therefore be necessary to have database of all these investigations to examine the patients in different stages of MM that actually have positive results with these laboratory modalities[21]. There are very few studies related to MM in this regard from India. This study therefore aims to describe the clinical profile in newly diagnosed cases of MM.[21]

AIMS AND OBJECTIVES

1) To study the clinical profile in newly diagnosed cases of Multiple Myeloma.
2) To study the molecular profile in newly diagnosed cases of Multiple Myeloma.

REVIEW OF LITERATURE

Multiple Myeloma (MM) is a malignant disorder characterized by uncontrolled proliferation of clonal plasma cells causing a wide variety of complications leading to organ dysfunction and eventually death. Since the report of the first case of myeloma by Solly in 1844 and the case of Thomas Alexander Mc Bean whose urine was examined by Henry Bence Jones, there has been a steady increase in the number of reported cases of MM.[22] Recently, there has been a dramatic improvement in our understanding of the pathogenesis of myeloma leading to major advances in the management of patients with MM. This review summarizes the latest advances in the diagnosis, staging, prognosis and management of MM incorporating results of major landmark trials and recent international consensus guidelines.[22]

Epidemiology

MM accounts for 10% of hematological malignancies. It evolves from a pre-malignant condition called monoclonal gammopathy of undetermined significance (MGUS). This is found in 3% of those over the age of 50,[23] and progresses to myeloma (or related disorders) at a rate of 1% per year.[24] Some have an intermediate stage (smoldering or asymptomatic myeloma) which carries a transformation risk of 10% per year for the first 5 years, 3% per year for the next 5 years, and 1% per year for the subsequent 10 years (cumulative probability of 73% at 15 years).[25] The median age at diagnosis is between 65 and 70 years. In Oman, there were 13 new cases of myeloma in 2009 (7 males and 6 females; all above the age of 50)[26]. Older age, immunosuppression and exposure to ionizing radiation, benzene, herbicides and insecticides have been reported as risk factors. The cause, however, remains unknown in most patients. The risk of developing MM is 4 folds higher in people with first degree relatives with myeloma and a small number of familial cases have been described[27].

ETIOLOGY

The cause of multiple myeloma is not clear.[27]

Environmental exposure:

The strongest environmental link to the cause of multiple myeloma is ionizing radiation, 29 people among the Nagasaki bomb survivors died of multiple myeloma. However, some recent studies do not confirm the increased risk of multiple myeloma among these people. However, the role of pesticides, chemicals, benzene, and smoking is supported by only epidemiological studies and there is no strong scientific evidence till date.[27]

Genetic predisposition:

The direct genetic link for multiple myeloma is not established, however the racial and gender predilection proposes a genetic component to the etiology. In the large scale multicentric study done by the Mayo clinic, 8 siblings had the disease, in a Sweden based study of multiple myeloma, the relative risk of inheritance in males was 3.86 if the father had Multiple Myeloma. Moreover, substantial family clustering was found in many cases. There is significant association of HLACw2 and HLACw5 to Multiple myeloma.[27]

Chronic Antigen stimulation:

Many M proteins have been shown to be antibodies against specific antigens, such as microbiological antigens, RBC antigens, neural antigens, lipoproteins, rheumatoid factors and coagulation factors. Chronic antigenic stimulation may predispose to the development of multiple myeloma as in cases of chronic osteomyelitis and cholecystitis. A recent case-controlled study suggested that females with silicon transplants have a higher risk for developing multiple myeloma.[27]

Virus:

Human herpes virus 8 has been found in the nonmalignant dendritic cells of bone marrow in patients with multiple myeloma. It's still not proven that they play a role in the malignant transformation of multiple myeloma.[27]

CYTOGENETICS

The malignant plasma cells carry complex chromosomal abnormalities that increase with disease progression. Microarray analysis has shed more light on sequential genetic changes from normal cells to myeloma cells and the multi-step progression from MGUS to multiple myeloma. Recent advances in cytogenetics have showed that IgH translocations and aneuploidy states could be the possible early signatures of multiple myeloma. The common translocations include, t(11;14), t(14;16), t(4;14), t(6;14). These IgH translocations are mediated by the VDJ recombination errors. These translocations may increase in frequency as the disease progresses and result in activation of cyclin D1, D2, D3 or myeloma set domains or fibroblast growth factor 3 genes[28]. These changes would trigger the initial malignant proliferation and help in survival of the malignant plasma cells. However, the disease progression is sustained by further chromosomal abnormalities, like p53 mutation, c-myc and RAS gene mutation. Probably these bizarre multiple genetic abnormalities make multiple myeloma still an incurable disease. Chromosome 13 translocations, p53 deletions, c-myc mutation are associated with poor prognosis. Thus, genetic analysis is not needed for diagnosis but definitely plays a role in assessing the prognosis.[28]

Chromosomal Abnormalities

Based on chromosomal analysis, the chromosome number pattern is a powerful prognostic factor in patients with MM. In general, loss of genetic material (such as hypodiploidy) in almost all malignancies is a marker of poor prognosis, whereas gains (such as hypodiploidy) are usually associated with better outcome. Most probably because hypodiploidy

cause loss of functions such as tumor suppressor functions, while hypodiploidy causes gain of function that do not always leads to interference with the cell cycle.[28]

Hypodiploidy

The incidence of hypodiploidy is about 10%[29]. The importance of hypodiploidy for overall survival in MM is unclear. An adverse effect of hypodiploidy in general may be due to monosomy of specific chromosomes, where the general hypodiploidy might be a confounding factor. However, correlations with adverse OS have been found in multivariate analysis independent of other aberrations[30].

Hyperdiploidy

Chromosomal abnormalities are present in nearly all cases of MM. There are two described different pathways for abnormalities that drive the cells into MM. The first is represented by hyperdiploidy and involves the chromosomes 3, 5, 7, 9, 11, 15, 19 and 21 and is seen in more than 30% of patients[31]. However, the concept that hyperdiploidy drives the MM evolution is not fully understood. The other one is based upon IgH translocation, especially located to chromosomal locus 14q32[32].

Immunoglobin heavy chain (IgH) aberrations

Any gene that is translocated to be fused to the enhancer of the IGH gene in a PC will be highly expressed[33]. Translocations to the IgH locus occurs in about 50% of MGUS, 60- 65% of intramedullary MM and in 70-80% in extramedullary MM[34], indicating a gain of more mutations throughout the development of the disease.

t(11;14) (q13;q32)

The most frequent translocation including 14q32 is t(11;14)(q13;q32) occurring in approximately 30% of MM patients leading to dysregulating of CCND1, and consecutive overexpression of cyclin D1[35]. MM patients with

t(11;14) have a higher tendency of a non-secreting disease, morphology of a “lymphoplasmacytic” type and occur in high frequency in IgM MM[36].

t(4;14), t(14;16) and t(14;20)

The second most common is t(4;14) (p16;q32), occurring in about 12-15% of MM patients leading to up-regulation of MMSET due to translocation of this gene to the IgH-locus at 14q32 and, in turn, up-regulation of the fibroblast growth factor receptor 3 gene (FGFR3)[37]. FGFR3 is a receptor tyrosine kinase[38] and is thus a possible target for therapy with receptor tyrosine kinase inhibitors[39]. t (14;16) (q32;q23) also causes overexpression of c-maf (musculoaponeurotic fibrosarcoma)[37] which is a protooncogene[40]. Another maf gene is the mafB which strongly correlates to t (14;20) (q32;q12), a translocation occurring in about 1-2% of all MM patients and is strongly associated with poor prognosis[41]. While patients with t(14;16) and t(14;20) have an equally aggressive disease as those with t(4;14)[42]; due to the lower frequency of t(14;16), its significance is conclusive only in larger studies[42]. So far, t(4;14) and t(14;16) translocations are considered to be specific for MM, no other known malignancy carries these aberrations. Less frequent translocations are t (6;14) (6p21,q32), t(8;14)(q24;q32) and t(14;20)(q32;q11).

Structural aberrations Chromosome 1

Structural aberrations of chromosome 1 are the most frequent ones in MM and are identified in 40-48% of all cases[31]. The most common aberration is gain of 1q21 which is seen in 40% of all newly diagnosed MM cases, and in about 70% of relapses[43] while it is quite rare in MGUS. Since gains of 1q are frequently seen at later stages of the disease, the locus is considered to play a pathogenic role in disease progression and gains are therefore associated with poor prognosis[43,44].

del (8p21)

Previous studies have linked molecular dysregulations originating from changes in the 8p21 region to various malignancies including mantle cell lymphoma[45] and B-cell lymphoma[46], and the loss of this region has been shown to have a negative effect on survival in head and neck cancers. Our group has previously reported that del (8p21), is an independent poor prognostic factor in MM and both progression free survival (PFS) and OS are adversely affected.[47]

del (8q24)

8q24 encodes the c-myc gene. Gene expression profiling studies have pointed out the MYC pathway as a key player in the evolution of normal PCs to MM[48]. The most well-known is t(8;14) (q24; q32) which is associated with Burkitt's lymphoma and NHL, and also described in MM.

Chromosome 13

Deletion of 13q or the whole chromosome 13, identified by FISH in less than 50% of the patients, has for many years been considered to be an adverse prognostic factor[49]. However, in the earlier studies the association with poor prognosis was based on conventional cytogenetics and in almost all new studies using FISH and multivariate analysis including other chromosomal abnormalities, the loss of 13q is not an independent prognostic factor.[50]

del (17p) (p53)

This abnormality is a strong predictor of extremely low OS and the lowest rate of achieving CR in comparison to other or no abnormalities[51]. Deletion of 17p is probably one of the most predictive molecular markers for resistance to therapy and short OS in MM identified so far[51]. Neither high dose therapy nor allogenic transplantation seems to overcome the dismal prognosis for patients with TP53 deletions/mutations[52].

Table 1: Incidence of Chromosomal Abnormalities in MM[28]

GenomicAberration	
del(13q)	~50
14q32Translocations	~50
Hyperdiploidy	~50
t(4;14)	~15
t(11;14)	~15
t(14;16)	~5
t(14;20)	~1
del(17p)	~10
gain(1q21)	~30-43
del(1p21)	~20

Pathogenesis of MM

The progression of MM begins with the asymptomatic, precursor pathogenic state of MGUS. Evidence indicates that MGUS, previously characterized by myeloma cell growth without bone destruction or other organ involvement, is in fact associated with alterations in the bone. Epidemiologic evidence has shown that patients with MGUS suffer from a significantly increased fracture risk, and that the prevalence of MGUS is increased in patients with osteoporosis.[53] Recent findings by Drake et al. have demonstrated that the onset of MGUS is concurrent with the deterioration of both axial and appendicular micro architecture leading to skeletal fragility.[53] The relationship between bone loss in MGUS and the progression to MM is an area of current interest, as the correlation may suggest that treating bone loss in MGUS could not only decrease fracture risk in these patients, but could also delay the onset of MM, a theory currently under investigation in our labs and others.[53]

In the absence of clinical symptoms, MGUS is diagnosed by quantifying the amount of immunoglobulin present in both the bloodstream and BM, specifically with a plasma cell population of <10% in the BM. With a

plasma cell content exceeding 10%, the disease state transitions into either smoldering MM (SMM) or MM (if clinically manifested).[54] MGUS progresses to MM at a rate of 1–2% of patients per year and this transition is likely influenced by the presence of mutational diversity or clonality of MM cell populations as well as changes in the local BM and other systemic factors.[54,55,56,57] MM cells are thought to initially create a plasmacytoma, a single tumor, and then develop into multiple lesions to form the disease of multiple myeloma.[58] Smoldering multiple myeloma (SMM) is an intermediate clinical stage between MGUS and MM. It is classified as having high serum or urinary monoclonal protein as well as clonal BM plasma cells in the range of 10–60%, in the absence of additional myeloma defining events[60] such as hypercalcemia, renal insufficiency, anemia, or bone lesions.[61]

With the evasion techniques of clonal evolution and drug resistance, MM may progress to an aggressive, bone-marrow independent disease known as plasma cell leukemia (PCL).[61.62] In PCL, MM cells proliferate and spread into circulation, causing an increase in plasma cells (≥20%) in the blood and often creating plasmacytomas at other places outside the BM throughout the body.[63] Efforts to fully understand the pathogenesis of both precursor, symptomatic, and terminal stage. MM should aim to identify mechanisms that cause somatic mutations, drug resistance, immune evasion, or relapse as potential drug targets. Treatments that interfere with MM growth and osteolysis in the bone marrow microenvironment (BMM) to slow disease progression and improve patient quality of life and life expectancy are already in use with additional treatments in development.[64]

Pathophysiology of the clinical presentation

The malignant cells produce monoclonal immunoglobulins or light chains. The expanding clone replaces the normal BM leading to anemia and other cytopenias. The malignant cells also cause inhibition of osteoblasts and stimulation of osteoclasts leading to the appearance of lytic bone lesions. This is mediated through an increase in RANKL (receptor activator of NFκB ligand), which stimulates osteoclasts and a decrease in its inhibitor osteoprotegrin (OPG). MIP-1 alpha (macrophage inflammatory protein-1 alpha) and IL-6 also stimulate osteoclasts. Increased levels of DKK1 (dickkopf 1) inhibit osteoblasts. Inhibition of osteoblasts explains why alkaline phosphatase levels are not increased and why radionucleotide bone scans are not helpful in these patients. The increase in osteoclastic activity also explains the hypercalcemia seen in these patients.[65]

Renal insufficiency in MM is mostly caused by cast nephropathy (tubular damage and obstruction resulting from binding of light chains to Tamm-Horsfall mucoproteins). Other causes include amyloidosis, light chain or heavy chain deposition disease, plasma cell infiltration and interstitial nephritis. Other potential causes include: volume depletion, hypercalcemia, hyper viscosity, nephrotoxic drugs (e.g. NSAIDs), contrast nephropathy, infections, bisphosphonates and hyperuricemia.[65]

The production of dysfunctional immunoglobulins, suppression of uninvolved normal globulins, abnormal lymphocyte function and leukopenia all lead to immunopanels and recurrent infections. High levels of immunoglobulins can lead to hyper viscosity (typically when serum viscosity is >5 centipoises) causing headache, blurring of vision or even coma. Accumulation of free light chains in tissues can lead to amyloidosis. Fig. 2.1 illustrates the pathophysiology of the different clinical manifestations in MM.[65]

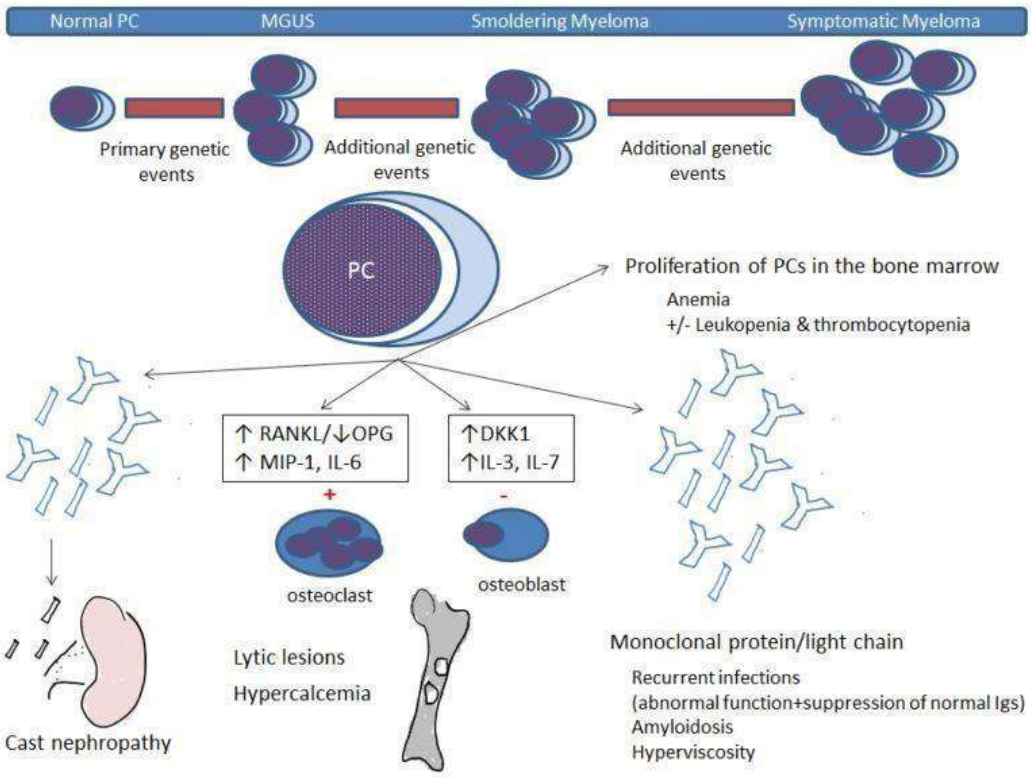

Figure 2: Pathophysiology of MM. PCs: plasma cells, RANKL: receptor activator of nuclear factor Kappa B ligand; OPG: osteoprotegrin; MIP-1: macrophage inflammatory protein-1 alpha; IL: inter-leukine; Igs: immunoglobulins.

Symptoms

Signs and symptoms of multiple myeloma can vary and early in the disease, there may be none.

When signs and symptoms do occur, they can include:

- Bone pain
- Nausea
- Constipation
- Loss of appetite
- Mental fogginess or confusion
- Fatigue

- Frequent infections
- Weight loss
- Weakness or numbness in lower limbs
- Excessive thirst

Diagnosis

The most common presenting symptoms of MM are fatigue and bone pain.[14]Anemia occurs in approximately 75% of patients and contributes to fatigue. Osteolytic skeletal lesions can be detected in approximately 80% of patients. Other common findings at presentation include hypercalcemia (15%), and elevated serum creatinine ≥2 mg/dL (20%).[14] Approximately 1 to 2% of patients with MM have extramedullary disease (EMD) at the time of initial diagnosis, while 8% develop EMD later on in the disease course.[66]

A monoclonal (M) protein in the serum or urine is a cardinal feature of MM, but is seen in only 82% of patients by serum protein electrophoresis.[1] The sensitivity increases to 93% when serum immunofixation is added, and to 97% with the addition of either the serum free light chain (FLC) assay or a 24 hour urine studies.[67] Thus if MM is suspected, the recommended screening strategy is to order serum protein electrophoresis, serum immunofixation, and either a serum FLC assay or a 24 hour urine protein electrophoresis with immunofixation. The M protein type is IgG in approximately 50%, IgA in 20%, immunoglobulin light chain only in 20%, IgD in 2%, and IgM in 0.5%.[1] About 2–3% of MM has no detectable M protein, and is referred to as non-secretory MM.[68]

The baseline diagnostic work up required for the diagnosis of MM includes complete blood count, serum calcium, serum creatinine, serum and urine protein electrophoresis with immunofixation, serum FLC assay, and bone marrow examination. In addition, low dose whole body computed tomography (CT), or fluorodeoxyglucose (FDG) positron emission tomography/CT (PET/CT), or at minimum, plain radiographs of the entire skeleton are required to detect osteolytic bone lesions.[69] The osteolytic

bone lesions in MM exhibit no new bone formation, and nuclear medicine bone scans are therefore not helpful.[70] Magnetic resonance imaging (MRI) of the whole body or spine/pelvis is needed in patients with suspected SMM, and whenever the diagnosis of MM is in doubt, to look for focal bone marrow lesions.[71] MRI scans are also often needed in patients with osteolytic bone disease involving the spine to rule out cord compression, and to determine the need for interventional procedures such as vertebroplasty or kyphoplasty.

Treatment of Relapsed Multiple Myeloma

The approach to treatment of relapsed MM is complicated. Numerous effective regimens are available, and the choice of treatment depends on numerous factors such as drug availability, response to prior therapy, aggressiveness of the relapse, eligibility for ASCT, and whether the relapse occurred on or off therapy. In eligible patients, ASCT should be included in the consideration if the patient has never had an ASCT, or if the remission duration with a prior ASCT exceeds 18 months (unmaintained) or 36 months (with maintenance).[72] Recent data support the use of a triplet for relapsed MM, but selected patients with indolent relapse can often be treated with a doublet such as Rd, or pomalidomide plus low dose dexamethasone (Pd). MM is characterized by relapses and remissions, with each remission typically lasting less than the previous one.[73] In the absence of toxicity, most regimens are continued until progression in the relapsed setting. However, in some regimens such as those employing bortezomib, carfilzomib, or alkylators it may be reasonable to stop therapy with these drugs once a stable plateau has been reached in order to minimize risks of serious toxicity.

New agents approved for the treatment of relapsed MM include carfilzomib, pomalidomide, and Panobinostat. The most common regimens and new drugs used in the treatment of relapsed refractory MM are discussed below.

Bortezomib and Lenalidomide based regimens

Rd is an effective regimen in relapsed MM, although the dose of dexamethasone must be reduced from the schedules used in the original pivotal trials.[74,75] Triplet regimens such as VRD, VCD, and VTD can also be used in the relapsed refractory setting, and are well tolerated when low dose dexamethasone and weekly subcutaneous bortezomib schedules are used.[76,77,78]

Carfilzomib and Pomalidomide based regimens

Carfilzomib is a keto-epoxide tetrapeptide proteasome inhibitor approved for the treatment of relapsed refractory MM in patients who have been previously treated with lenalidomide and bortezomib.[79] In a phase III trial of 792 patients, carfilzomib, lenalidomide, dexamethasone (KRd) were associated with better response rates, PFS, and OS compared with Rd.[80] PFS was 26.3 months with KRD versus 17.6 months in the control group; P=0.0001. The 2-year survival rates were 73.3% and 65.0%, respectively, P=0.04. Based on these results, KRd is now an important option for the treatment of relapsed MM. There is debate about whether KRd (or similar carfilzomib based regimen) should be used ahead of bortezomib-based regimens in relapsed MM. Support for carfilzomib as a more potent proteasome inhibitor than bortezomib comes from a randomized trial in which carfilzomib/dexamethasone demonstrated a doubling of PFS compared with bortezomib/dexamethasone in relapsed MM; PFS 18.7 months versus 9.4 months, respectively, P<0.001.[81] However, the dose of carfilzomib used in this trial (56mg/m^2) was twice the approved dose, and carries a much higher cost compared with bortezomib. Further the dosing of bortezomib used in this trial was suboptimal (twice-weekly schedule) making it difficult to make definitive conclusions. Carfilzomib does have lower risk of neurotoxicity than bortezomib, but a small proportion (5%) of patients may experience serious cardiac side effects.

Pomalidomide is an analog of lenalidomide and thalidomide approved for the treatment of relapsed refractory MM. It has significant activity in relapsed refractory MM, even in patients failing lenalidomide,[82,83] or lenalidomide and bortezomib.[84] In a randomized trial of 302 patients with refractory MM, Pd was found superior to high-dose dexamethasone (median PFS 4.0 months versus 1.9 months, respectively, P<0.0001).[85] As with Rd, the doublet regimen of Pd is a reasonable option for patients with indolent relapse. But more often, pomalidomide needs to be administered in combinations such as pomalidomide, cyclophosphamide, prednisone (PCP), pomalidomide, bortezomib, dexamethasone (PVD), or carfilzomib, pomalidomide, dexamethasone (car/pom/dex).

Panobinostat

Panobinostat is a pan-deacetylase inhibitor approved in 2015 for the treatment of relapsed and refractory MM.[86] It is the first agent from a new class of drugs with meaningful clinical activity in MM in nearly 15 years. Its putative mechanism of action is to block the aggresomal pathway, an alternative route for cells to bypass the lethal effects of proteasome inhibition. By combining bortezomib and Panobinostat, there is simultaneous blockade of both proteasome and aggresomal pathways.[87,88] In a randomized trial of 768 patients, bortezomib/dexamethasone plus Panobinostat was associated with superior PFS compared with bortezomib/dexamethasone plus placebo (median PFS 12 months versus 8·1months, respectively, P<0.0001).[89] However, Panobinostat therapy was associated with grade 3 diarrhea in approximately 25% of patients, and care should be exercised when using this drug. We recommend a lower dose than the approved starting dose. We also recommend that bortezomib be used in the once-weekly subcutaneous schedule rather than the twice weekly regimen used in the pivotal trial.[89,90,91]

Liposomal Doxorubicin

Anthracyclines have marginal single-agent activity in MM. A phase III randomized trial found that median time to progression (TTP) was superior with bortezomib plus pegylated liposomal doxorubicin compared with bortezomib alone, 9.3 months versus 6.5 months, respectively, P<0.001.[92] OS at 15 months was also superior, 76% compared with 65%, respectively, P = 0.03. Despite this study, liposomal doxorubicin is infrequently used in the treatment of relapsed MM given availability of other active agents.

Monoclonal antibodies

Two monoclonal antibodies (Daratumumab and SAR650984) targeting CD38 have shown promise in relapsed, refractory MM. In a phase II trial, Daratumumab as a single-agent produced a response rate of approximately 30% in heavily pre-treated patients.[93] These are very encouraging results and we are optimistic that Daratumumab will be approved for use in relapsed refractory MM based on these data.

Elotuzumab, a monoclonal antibody targeting the signaling lymphocytic activation molecule F7 (SLAMF7), has also shown activity in relapsed MM.[25] Unlike anti-CD38 antibodies, Elotuzumab does not appear to have any single-agent activity. However, it appears to have synergistic activity when combined with Rd. In a phase III trial of 646 patients, Elotuzumab plus Rd was superior to Rd in terms of PFS, median PFS 19.4 months versus 14.9 months, respectively, P<0.001.

Elotuzumab is also well tolerated, and is expected to gain approval within the next few months.

Ixazomib

Ixazomib is an oral proteasome inhibitor that is active in both the relapsed refractory setting and in newly diagnosed MM. In a randomized controlled trial in relapsed MM, Ixazomib, Lenalidomide, Dexamethasone (IRd) was

found to improve PFS compared with Rd.[94] Based on these results it is anticipated that Ixazomib will secure regulatory approval soon. It has the advantage of once weekly oral administration. Compared with Bortezomib it has more gastrointestinal adverse events, but lower risk of neurotoxicity.

Other Emerging Options

Other promising agents include Marizomib, a new proteasome inhibitor, Oprozomib, an oral proteasome inhibitor related to Carfilzomib; Filanesib, a kinesin spindle protein inhibitor; Dinaciclib, a cyclin dependent kinase inhibitor; ABT-199, a selective BCL-2 inhibitor, and LGH447, pan PIM kinase inhibitor. Each of these has shown single agent activity in relapsed MM.[94]

Prognostic factors in Multiple Myeloma

Multiple Myeloma is a type of blood cancer that affects plasma cells in the bone marrow. Prognostic factors are variables that can predict the course of a disease and the likelihood of a positive outcome.

Several studies have identified various prognostic factors in multiple myeloma, including:

- International Staging System (ISS) stage: Patients with lower ISS stages have a better prognosis than those with higher stages.[95]
- Cytogenetics: Patients with certain genetic abnormalities, such as deletion of chromosome 17p or t(4;14), have a worse prognosis than those without these abnormalities.[96]
- Serum lactate dehydrogenase (LDH) levels: Elevated LDH levels are associated with a worse prognosis.[97]
- Beta-2-microglobulin levels: Elevated Beta 2 microglobulin levels are associated with a worse prognosis,[98]
- Age: Older patients tend to have a worse prognosis than younger patients.[97]

- Performance status: Patients with a better performance status tend to have a better prognosis than those with a worse performance status[95].
- Hemoglobin levels: Low hemoglobin levels (anemia) are associated with a worse prognosis[98].

It is important to note that these are only some of the prognostic factors identified in multiple myeloma, and that treatment and overall prognosis are determined by various factors.

For many years, the factors contributing to the highly variable prognosis in myeloma were unclear. Early on, immunoglobulin isotype was shown to play a role in prognosis, with monoclonal IgA production (21%) associated with a worse prognosis[99]. The degree of plasma cell burden is only an issue in plasma cell leukemia.[100]

In 1975, the Durie-Salmon staging system was adopted, stratifying individuals by relative plasma cell burden (anemia), hypercalcemia, number of lytic lesions visible on X-ray, and serum urine M protein levels.[101] However, the number of lytic lesions on X-ray is observer dependent and created challenges with respect to enrollment and reproducibility between trials.

Thirty years later in 2005, Griepp and colleagues established the international staging system (ISS), utilizing the beta-2 macroglobulin level and albumin level to appropriately risk-stratify patients. The ISS can predict EFS and OS regardless of age, geographic region, study site, standard-dose vs. high-dose therapy (HDT), or the use of novel agents.[102]

Discovery of specific cytogenetic abnormalities correlates with prognosis in multiple myeloma and overall survival. Plasma cells typically have a low-proliferative index, and so cytogenetic abnormalities are detected in a small number of patients. Interphase FISH was found to be useful in identifying specific cytogenetic aberrations.[103]

Staging of Multiple Myeloma

Multiple Myeloma (MM) prognosis includes numerous tumor- and patient-specific factors. The International Staging System (ISS), published in 2005, is a simple tool that correlates MM prognosis and survival. Criteria for the three stages are based on levels of serum beta-2 macroglobulin and albumin[104]. Over the past decade, the understanding of cytogenetics and its influence on survival have added to the prognostic factors for myeloma, which were lacking in the original ISS. In 2015, the IMWG published a Revised ISS that incorporates cytogenetic factors and lactate dehydrogenase—a marker reflective of tumor burden—to the original ISS definitions of stage.[104]

Stage	Criteria	Survival (mo)
I	• β_2-microglobulin <3.5 mg/L • Albumin ≥3.5 g/dL *and* • Standard-risk chromosomal abnormalities *and* • Normal LDH (defined as less than ULN)	82
II	• Not R-ISS stage I or III	62
III	• β_2-microglobulin ≥5.5 mg/L regardless of albumin levels *and* • High-risk chromosomal abnormalities: del 17p, t(4;14) or t(14;16) *and* • High LDH (defined as higher than ULN)	40

del: deletion; LDH: lactate dehydrogenase; MM: multiple myeloma; R-ISS: Revised-International Staging System; t: translocation; ULN: upper limit of normal.

Figure3: R-ISS Staging of MM

REVIEW OF RELATED LITERATURE

Athira et al., (2008)[105] conducted a study to explore the clinical profile of multiple myeloma at GRH Madurai. The study reported that majority (53.8%) of patients belonged to 40–60-year age group with majority of male subjects. Backache was the most common presenting symptom, was present for minimum of 6.5 months. 65.4% of patients had a serum albumin of 3.0gm/dl and less, only 44.6% of patients had a serum albumin greater than 3.0gm/dl. Anemia (Hb< 12gm/dl) is present in all the patients, 76.9% had hemoglobin of less than 8.5gm/dl. The incidence of anemia is comparatively higher in patients. There is a definite correlation with bone marrow plasmacytosis and serum albumin. There is a definite correlation with bone marrow plasmacytosis and serum albumin. The incidence of renal failure in patients is comparable to the world statistics.

Lee et al., (2012)[106] conducted a study on the incidence of multiple myeloma (MM) is known to be variable according to ethnicity. However, the difference of clinical characteristics between ethnic groups is not well-defined. In Asian countries the incidence of MM has been lower compared with Western countries. However, there are growing evidences that MM is increasing very rapidly in this region. Until now, only few data of Asian patients have been reported. Asian myeloma network decided to analyze the first multinational project to explore clinical characteristics of Asian MM patients and clinical practice performed in Asian countries. Data was collected from 21 centers from 7 countries retrospectively. Clinical characteristics of 2,969 symptomatic MM patients at diagnosis were described. Overall survival (OS) and prognostic factors were analyzed for 2,273 patients who had survival data. Median OS was 54 months (95% CI 48.0-60.0). Patients who were diagnosed before 2000 had shorter survival. Transplantation was performed to 513 patients with better survival (84 vs. 45 months, p<0.001). First line treatment of 2339 evaluable patients were analyzed. Overall response rate was 71% with

30%, VGPR or better. New drugs including bortezomib, thalidomide or lenalidomide were combined for 32.5% of all 2,339 patients without difference in response rate or OS according to combination. We successfully described clinical characteristics of Asian MM patients and this project will be the base for future studies or clinical trials for Asian MM patients. Updated analyses and comparison with Western data will be presented. AMN, supported by the International Myeloma Foundation (IMF) IMWG initiative.

Kaur et al., (2014)[107] conducted a study to explore clinical and pathological profile of multiple myeloma. This study reported that multiple myeloma comprised 11.1% of all hematological malignancies. The mean age was 58.8 years. Bony pain was the most common presenting complaint. Other findings were anemia, raised serum creatinine levels, high serum lactate dehydrogenase and C-reactive protein levels. Plasmolytic morphology was seen in 60% patients with diffuse marrow involvement being the most common pattern. The percentage incidence of Multiple Myeloma, out of all hematological malignancies reported in our study is comparable with other studies as regards to the median age of incidence, male to female ratio, clinical presentation and percentage of M band positivity. However, a higher percentage of our patients had hypercalcemia, higher serum lactate dehydrogenase levels and C – Reactive protein positivity and more lytic lesions. This corresponds with a higher tumor cell burden and a more frequent diffuse pattern of bone marrow involvement in our study group. This could be due to the smaller size of our study group, or due to late referral of patients to our tertiary care hospital.

Diwan et al., (2014)[108] Conducted a study to analyze the clinical and laboratory features of multiple myeloma (MM). A cross-sectional study of 20 newly diagnosed patients with MM over a period of 1 year in a tertiary health-care center. Based on Salmon-Durie criteria, newly diagnosed 20

patients of MM were selected for the study. Routine hematological and biochemical investigations, bone marrow examination, serum protein electrophoresis and urine for Bence Jones protein were done. Radiological investigations conducted to look for osteolytic lesions, extramedullary involvement and other pathologies. Out of total 20 patients, 10 were males and 10 were females with sixth decade as the common age group at presentation. Common clinical symptoms were bone pains, localized body swelling, fever, generalized weakness and fatigue and motor weakness of lower limbs. Clinical examination revealed pallor in 80% patients, bony tenderness in 85% patients and 55% patients presented with infections. All patients had a presence of M band on serum protein electrophoresis, whereas 30% patients had urinary Bence Jones protein positive. Among skeletal system spine and skull were the common sites of involvement 60% and 55%, respectively. Nearly, 85% patients had osteolytic lesions. Among 20 patients, various clinical presentations observed were infections, renal impairment, paraplegia and extramedullary plasmacytosis in addition to anemia and bony pains

Lu et al., (2014)[109] The aim of this study was to understand the clinical features and treatment outcome of Chinese patients with multiple myeloma (MM). This retrospective study enrolled 940 newly diagnosed inpatients (median age, 59 years; immunoglobulin (IgD isotype, 6.5%) with complete follow-up data at three centers. In all, 85.8% of patients were of Durie-Salmon stage III and 48.3% were of International Staging System (ISS) stage III at diagnosis. Also, 9.6% of patients had extramedullary plasmacytoma. Compared with IgG, IgD-type patients were diagnosed at a younger age, and more patients were of ISS stage III, with hypercalcemia, elevated levels of lactate dehydrogenase, hyperuricemia, renal dysfunction and 1q21 amplification (P=0.03). The overall survival (OS) benefit was more prominent in IgG than in IgD when patients received bortezomib; however, they showed no significant difference when they received older therapies such as melphalan combined with

prednisone or vincristine combined with adriamycin and dexamethasone. Fluorescence in situ hybridization (FISH) results showed that 17.6% had 17p13 deletion. Conventional cytogenetics revealed that 13.3% were hypodiploid and those cases had the worst survival, but hyperdiploid cases (9.3%) did not show any survival benefit compared with those with a normal karyotype (77.4%). Median OS and progression-free survival for all patients were 54 and 26 months, respectively. Significant factors for survival by multivariate analysis were gender, ISS stage, number of FISH abnormalities and extramedullary disease. MM in mainland China presents with different features, with patients being of younger age and having higher risk and more survival benefit in IgG patients receiving bortezomib.

Pegu et al., (2016)[110] conducted a study to describe the common clinical and laboratory features, stages and outcome of patients with Multiple Myeloma coming to a Tertiary Care Center in North East India. Newly diagnosed and previously diagnosed untreated patients of MM coming to Assam Medical College over a period of one year were randomly included in this prospective observational study. 44 Multiple myelomas mostly from 5th and 6th decade with the age varying from 38 to 82 and a mean age of 57.7 years (SD 10.29); 27 (61%) patients were male and 17 (39%) were females with a male-to-female ratio of 1.6:1; 38 (86%) presented with backache and other bone pains, 35(80%) had generalized weakness and easy fatigability, 13 (30%) had symptoms of spinal cord compression, 14 (32%) had fever. On examination 37 (84%) had pallor, 34 (77%) had bony tenderness, 14 (32%) had paraplegia; 40 (91%) cases revealed positive M Band by serum protein electrophoresis. In rest of the 4 cases, band was determined by immunofixation method. Urinary Bence-Jones protein was estimated in 28 out of 44 patients and out of them 4 (14%) were positive. 40 (91%) out of 44 patients had radiologically detectable abnormalities; 35 (80%) had lytic lesions, 17 (39%) had pathological fractures, 21 (48%) had generalized osteoporosis and only 4(9%) had normal skeletal survey. Out

of 35 cases of lytic lesions, most frequent area was spine in 25 (71%); 7 (16%) cases were found to be in stage I, 20 (45%) were found to be in stage II and 17 (39%) were in stage III. The study concluded that though most patients were in sixth decade, but we got significant involvement in younger age group. Bone pain, mostly low backache was the most common presenting symptom along with fatigue and weakness. Majority of patients were in higher stages (ISS II, III) at the time of diagnosis and severe anemia, lytic lesions, pathological fractures and renal insufficiency were most observations in these patients in higher stages.

Muzamil et al., (2016)[111] Explained that Plasma cell dyscrasias represent 1.4–2% of all malignancies and among hematologic malignancies; it constitutes 10% of the tumors. Plasma cell dyscrasias are composed of multiple myeloma (MM), and primary and secondary plasma cell leukemia. Primary plasma cell leukemia (pPCL) is a rare and aggressive disease, representing 1– 4% of plasma cell dyscrasias. RESULTS: The prognosis of this is very poor with median survival of 8–11 months in different reported series. DISCUSSION: We are reporting a study from our hospital over a period of 8 years and 9 months, in which pPCL was found in 1.8% of MM patients, with slight male predominance and earlier age than MM, and all had high disease burden with high lactate dehydrogenase (LDH), β2-microglobulin, and plasmacytosis. This disease had very aggressive behavior, especially with light chain lambda disease, and all patients succumbed within 8 months of treatment.

Fousad et al., (2018)[112] Conducted a study on the incidence of multiple myeloma (MM) is known to be variable according to ethnicity and is increasing rapidly in Asian countries. Because of huge disparities in economy, lack of adequate health-care infrastructure and the lack of access to novel drugs in our country, treatment of multiple myeloma is still a challenge to medical field in India. This was a descriptive longitudinal study conducted in the medicine and oncology units of a tertiary care

hospital in south India. During the one-year period of data collection, 37 cases of multiple myeloma were diagnosed, of which 5 cases were excluded. The diagnosis of MM was made based on the International Myeloma Working Group: Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders. The clinical and laboratory characteristics, and treatment were studied. The male to female ratio was 1.3:1. The commonest symptoms noticed were fatigue 32 (100%) and bone pain 31 (96.9%). 6 (18.8%) patients had hypercalcemia and 7 (21.9%) patients had elevated serum creatinine levels. 29 (91%) out of 32 had lytic lesions in the skull and 27 (84%) had lytic lesions in the spine. One patient expired during the course of the treatment. 20 (64%) out of 32 patients had partial response to treatment, 7 (23%) had complete response and 4 (13%) of them had stable disease not responding to treatment. To conclude, the patients with multiple myeloma in the present study had a male preponderance. Most common symptoms noticed were fatigue and bone pain and majority had spine tenderness on examination. The presentation of MM is non-specific and patient can come with varied presentations at onset. The quality of life and survival in MM patients can be improved significantly if there is access to newer therapies.

Chowdhury (2018)[113] The aim of this study was to define and evaluate the clinico-laboratory features of newly diagnosed adult multiple myeloma (MM) patients in the context of Bangladesh. This study was carried out in two centers, from October 2005 to January 2010 in Bangabandhu Sheikh Mujib Medical University (BSMMU) and July 2012 to June 2017 in Enam Medical College and Hospital (EMCH). Thirty two diagnosed valid cases of multiple myeloma were included in this study. Clinical history, physical and relevant laboratory findings were carefully recorded and analyzed. In this study among 32 patients, 29 were males and 3 were females with mean age 51±10.09 years[94]. The common complaints were bone pain, weakness and fatigue. The common clinical findings were bone

tenderness, pallor and high ESR (ESR of all the study patients was more than 100 mm/hr). Hemoglobin level was <8.5 gm/dL in 13 patients, serum creatinine ≥2 mg/dL in seven patients, serum albumin <3.0 gm/dl in 14 patients and serum β2 microglobulin >5.5mg/L in 15 patients. Three patients were hypercalcemic. Lytic lesions were the most common radiological finding in the study. This study showed that multiple myeloma is a disease of the middle and elderly aged population with male preponderance, with high male to female ratio. Multivenue studies are needed to view the real picture of multiple myeloma in the context of Bangladesh.

Shah et al., (2018)[114] Explained that Robust establishment of survival in multiple myeloma (MM) and its relationship to recurrent genetic aberrations is required as outcomes are variable despite apparent similar staging. We assayed copy number alterations (CNA) and translocations in 1036 patients from the NCRI Myeloma XI trial and linked these to overall survival (OS) and progression-free survival. Through a meta-analysis of these data with data from MRC Myeloma IX trial, totaling 1905 newly diagnosed MM patients (NDMM), we confirm the association of t(4;14), t(14;16), t(14;20), del(17p) and gain(1q21) with poor prognosis with hazard ratios (HRs) for OS of 1.60 (P=4.77 × 10(-7)), 1.74 (P=0.0005), 1.90 (P=0.0089), 2.10 (P=8.86 × 10(-14)) and 1.68 (P=2.18 × 10(-14)), respectively. Patients with 'double-hit' defined by co-occurrence of at least two adverse lesions have an especially poor prognosis with HRs for OS of 2.67 (P=8.13 × 10(27)) for all patients and 3.19 (P=1.23 × 10(-18)) for intensively treated patients. Using comprehensive CNA and translocation profiling in Myeloma XI we also demonstrate a strong association between t(4;14) and BIRC2/BIRC3 deletion (P=8.7 × 10(-15)), including homozygous deletion. Finally, we define distinct sub-groups of hyperdiploid MM, with either gain(1q21) and CCND2 over expression (P<0.0001) or gain(11q25) and CCND1 over expression (P<0.0001).

Hussain et al., (2019)[115] The purpose of the retrospective study was to assess the hematological profile, different biochemical parameters, and the serum electrophoresis patterns of patients consistent with clinical symptoms of multiple myeloma. A retrospective study of 99 patients diagnosed with multiple myeloma (MM) was carried out at the Hematology Department of Benghazi Medical Center (BMC) in Benghazi, Libya from January 2010 to March 2017. Information on the laboratory features was obtained at presentation (before treatment) and analyzed. Results: Of the 99 study detected cases of multiple myeloma at diagnosis, 14% were younger than 45 years and 35% were 70 years or older. The mean age was 61 years, of which 42 (42.4%) were males and 57 (57.6%) were females. Anemia was seen in roughly half of the diagnosed cases, most of which was normocytic normochromic anemia. High erythrocyte sedimentation rate (ESR) was seen in 65.3% of cases and increased neutrophil-to-lymphocyte ratio (NLR) was seen in 29.7%. Other abnormal serum levels with regard to the cases are as follows: hyperproteinemia in 30%, low albumin/globulin (A/G) ratio in 54.2%, hypercalcemia in 11.3%, serum creatinine level of >2.0 mg/dL in 27.2% cases, and increased β2-microglobulin in 67%. Serum protein electrophoresis revealed a localized band in 70.8% of patients. Monoclonal bands were seen in 44 cases (95.7%) and a bi-clonal pattern in two cases (4.3%), 78% of M-band showed migration to γ-region of electrophoretogram and 18% to β-region. Hypogammaglobulinemia was detected in 32.8% and hypergammaglobulinemia was detected in 49.2%. Of the hypergammaglobulinemia, 18.1% showed polyclonal gammaglobulinemia. Bence Jones protein was positive in 50% cases. IgG was the commonest type, followed by IgA then light chain. In 26.5% of cases, the only diagnosis was multiple myeloma. Light chain multiple myeloma patients had high α2 globulin concentration and normal A/G ratio. Apart from the diagnosis of multiple myeloma, a number of cases had varying diagnoses including the following: 4% non-secretory myeloma, 2% amyloidosis with

nephrotic syndrome, 2% liver cirrhosis, and 18.2% renal failure. Most patients presented in stage III. The presence of anemia, high ESR, and low A/G ratio in elderly patients should alert the clinician to investigate along the lines of multiple myeloma. In this study, unfortunately, the laboratory investigations were insufficient for diagnosing this disease in most patients. Most patients were diagnosed at stage III. Absence of paraprotein in the blood does not exclude multiple myeloma. It was further observed that most of the patients presented with significant renal damage, which attributed to hyperuricemia, hypercalcemia, or high NLR. Multiple causes of renal failure occur in myeloma and are often present at the time of diagnosis.

Alhuqayl et al., (2019)[116] This study was performed to assess the clinical features of Saudi MM patients. Patients and Methods: Data were collected retrospectively from the medical records of patients between November 2014 and September 2017 at King Khalid University Hospital, Riyadh, Saudi Arabia. During the study period, MM was diagnosed among 36 patients (mean age- 65.2 ± 11.2 years) comprising of 19 females and 17 males of Saudi nationality. Out of the 19 female patients, 15 (78.9%) had κ chain restriction, whereas among the 17 male MM patients, 14 (82.3%) had λ light-chain restricted disease. All the patients (100%) had anemia (median 93 g/L; interquartile range [IQR] 22.5), 35/36 (97.2%) patients had increased red cell distribution width (RDW) (median 18.3%; IQR 4.5), 34/36 (94.4%) patients had increased monocyte percentage (median 13.7%; IQR 3.4), and 34/36 (94.4%) patients had diabetes mellitus. Gender preferences for κ and λ light chain among MM patients and the association of increased RDW with MM require validation in large-scale studies.

Mohammed et al., (2019)[117] stated that Multiple myeloma (MM) is slowly becoming a huge medical burden, challenging the health-care systems of Asian countries. The study was conducted in a tertiary health care centre

over a span of 3 years and 94 patients diagnosed as MM with complete workup including beta2 microglobulin (β2M), bone marrow plasma cell percentage, serum protein electrophoresis, serum and urine Immunofixation and serum Free Light Chains (FLC) were included. The study found a male to female ratio of 1.47:1. The mean age of patients was 55.5±11.78 yrs. Backache was the most frequent presentation (30%) of the patients followed by generalized weakness (22%). The percentage of plasma cells, hemoglobin, urea, creatinine, uric acid, calcium and β2M showed significant difference across the stages. 38.3% of the patients were in stage III, 29.8% in stage II and 31.9% in stage I. IgGκ type constituted 70%, other fraction being IgGλ (10%), IgMκ (10%), IgAκ (5%) and IgAλ (5%). M band was not seen in 11% of patients. The presentation of MM is nonspecific and patient can come with varied presentations at onset. We have biochemically characterized the three stages of MM and this will form a basis for further larger studies on these lines and to develop stage-based algorithms for early and better diagnosis and prognosis of MM.

Seesaghur et al., (2021)[118] Patients with multiple myeloma (MM) experience significant delays in diagnosis due to non-specific symptomatology. The aim of this study was to characterize the frequency and timing of clinical features in the primary care setting prior to MM diagnosis. Population based cohort study. Electronic health records data of approximately 17 million patients (2006-2016) within the UK Clinical Practice Research Datalink. Participants: Patients aged ≥18 years with newly diagnosed MM (NDMM), no history of solid tumors and ≥2 years registration in a primary care practice prior to MM diagnosis. Main outcome measures: Clinical features and symptoms including bone pain, skeletal-related events (SREs), investigation and confirmation of MM diagnostic CRAB criteria (hypercalcemia, renal impairment, anemia, bone lesions) during the 2 years prior to MM diagnosis; time between symptom manifestation and/or relevant investigation and diagnosis of MM. Among

2646 patients with NDMM, 47.5% had a bone pain record during the 2-year period prior to MM diagnosis, mainly affecting the back. Regardless of baseline bone pain, investigations for serum calcium level were used in 36.4% of patients prior to MM diagnosis, followed by hemoglobin (65.6%) or renal function (74.1%). Median (Q1, Q3) time from first- recorded bone pain to MM diagnosis was 220 (80, 476) days. Median (Q1, Q3) time from first- recorded hypercalcemia, renal impairment or anemia to MM diagnosis was 23 (12, 46), 58 (17, 254) and 73 days (28, 232), respectively. An imaging investigation or referral for imaging was recorded for 60.0% of patients with bone pain/SRE and 32% without. Conclusions: Nearly half of patients diagnosed with NDMM presented with bone pain approximately 7 months prior to MM diagnosis. Investigations to evaluate all CRAB criteria, including targeted imaging, were underused. Early recognition of myeloma clinical features and optimised use of investigations in primary care may potentially expedite MM diagnosis.

Singh et al., (2022)[119] conducted a study to study the various parameters and its incidence in Multiple Myeloma patients. This is a cross sectional study conducted in the department of medicine and oncology of tertiary care hospital of North India. The study reported that Multiple Myeloma was most common in 5th decade with male predominance and more common in urban population. Most common symptom was bone pain (63%) and weight loss (9%) was least common. 65% had anemia, 18% had renal insufficiency and 34% had hypercalcemia. All of the patients had M-band in gamma globulin region with 48% had ISS stage 1. 70(70%) had lytic lesions in the skull. The study concluded that majority of the patients of Multiple Myeloma were males and majority were farmers. Majority of patients were from urban area. Bone pain being the most common symptom followed by the fatigue. Anemia and hypercalcemia were less common in our study population. Most of the patients had ISS stage 1. The presentation of MM varies among patients and with adequate

health infrastructure better outcome and early diagnosis of multiple myeloma will be there.

METHODS AND MATERIALS

SOURCE OF DATA

The study was conducted in the Department of Medicine, Department of Oncology and the Allied Specialties of Medicine of DMCH, Ludhiana.

METHOD OF COLLECTION OF DATA

Inclusion Criterion:

1. Newly diagnosed cases of multiple myeloma [inpatients and outpatients].
2. The patients who gave the consent for the study.

Exclusion Criterion:

1. K/c/o multiple myeloma on follow up.
2. Patients who did not give the consent for the study.
3. Monoclonal Gammopathies of undetermined significance [MGUS].
4. Plasma cell leukemias.

1. The patients who were newly diagnosed with Multiple Myeloma on the basis of revised IMWG diagnostic criteria 2014 were enrolled for the study.
2. A prospective observational study was performed on all the patients.
3. Patients were explained about the nature of the study and a written consent was taken.
4. Information was collected through a predesigned Performa for each patient enrolled into the study.
5. Detailed history was taken and examination was done.
6. Laboratory parameters to be evaluated were collected from patient's medical records.
7. Molecular workup done in the newly diagnosed cases was collected from patient's records**.**

Panel: Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and shouldering multiple myeloma

Definition of multiple myeloma

Clonal bone marrow plasma cells ≥10% or biopsy-proven bony or extramedullary plasmacytoma and

Any one or more of the following myeloma defining events [MDEs]:

1. Evidence of end organ damage [CRAB lesions] that can be attributed to the underlying plasma cell proliferative disorder, specifically:

- Hypercalcemia: serum calcium >0.25 mmol/l (>1 mg/dl) higher than the upper limit of normal or >2.75 mmol/l (> 11 mg/dl)
- Renal insufficiency: creatinine clearance <40 ml/min or serum creatinine >177 mmol/l (> 2 mg/dl)
- Anemia: hemoglobin value of >2 gm/dl below the lower limit of normal, or a hemoglobin value < 10 gm/dl
- Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT

2. Any one or more of the following biomarkers of malignancy (MDEs):
   - Clonal bone marrow plasma cell percentage ≥60%
   - Involved: uninvolved serum FLC ratio ≥100 (involved FLC level must be at least 100 mg/l)
   - >1 focal lesion on MRI studies (at least 5 mm in size)

Definition of smoldering multiple myeloma

Both criteria must be met:

- Serum monoclonal protein (IgG or IgA) ≥30 g/l or urinary monoclonal protein ≥500 mg per 24 h and/or clonal bone marrow plasma cells 10–60%
- Absence of myeloma defining events or amyloidosis

Revised International Staging System

STAGE I

- Serum albumin >3.5 g/dl
- Serum B2-microglobulin < 3.5 mg/l
- No high-risk cytogenetic features
- Normal serum lactate dehydrogenase level

STAGE II

Neither stage I nor stage lll

STAGE III

- Serum B2-microglobulin ≥ 5.5 mg/l
- AND one of the following: (a) High-risk cytogenetic features : t(4:14)

  t(14;16)

  del(17p)

(b) Elevated serum lactate dehydrogenase level

The clinical heterogeneity of Multiple Myeloma is dictated by the cytogenetic aberrations present in the clonal plasma cells (PCs). Cytogenetic studies in MM are hampered by the hypo proliferative nature of plasma cells in MM. Therefore, fluorescence in situ hybridization (FISH) analysis is an attractive alternative for evaluation of numerical and structural chromosomal changes in MM. In contrast to conventional cytogenetic, interphase fluorescence in situ hybridization (FISH) can detect cytogenetic abnormalities independent of cell proliferation. As such, the sensitivity of FISH is higher than conventional cytogenetic.

Heparinised bone marrow blood sample was taken and Plasma cells were counted from bone marrow smears and fluorescence-in-situ hybridization

(FISH) was performed using various probes as described below for each of the genetic abnormality. Number of cells analyzed per probe – 100 cells.

1. Zytolight SPEC Orange TP53/ CEN 17 SPEC Green DC DNA probe [for p53 deletion]
2. Zytolight SPEC FGFR3/ IGH Dual Colour Dual Fusion Probe [for t(4;14)]
3. Zytolight SPEC CCND1/ IGH Dual Colour – Dual Fusion Probe [for t(11;14)]
4. Zytolight SPEC MAF / IGH Dual Colour – Dual Fusion Probe [for t(14;16)]

Duration of Study / Number of Cases: All the patients of newly diagnosed MM during 1 year period [March 2021-February 2022] were enrolled for the study.

Outcome:

Indoor – Discharged /DAMA/ Death

Treatment started – Yes / No

Outdoor – Treatment started – Yes / No

Statistical Analysis:

Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATIONS & RESULTS

The study was conducted in the Department of Medicine, Department of Oncology and other Allied Specialties of Medicine in DMC & Hospital Ludhiana. 62 newly diagnosed cases of multiple myeloma diagnosed between 1st March 2021 and 28th Feb 2022 were included in the study from bothindoor and outdoor departments of the hospital.

TABLE 2 SEX DISTRIBUTION

Total number of patients - 62

Sex	Number Of Patients	Percentage
Male	36	58.1%
Female	26	41.9%

In our study it was observed that majority of patients were males i.e 36 out of 62 patients weremales [58.1%] and 26 were females [41.9%].

FIGURE 4- SEX DISTRIBUTION

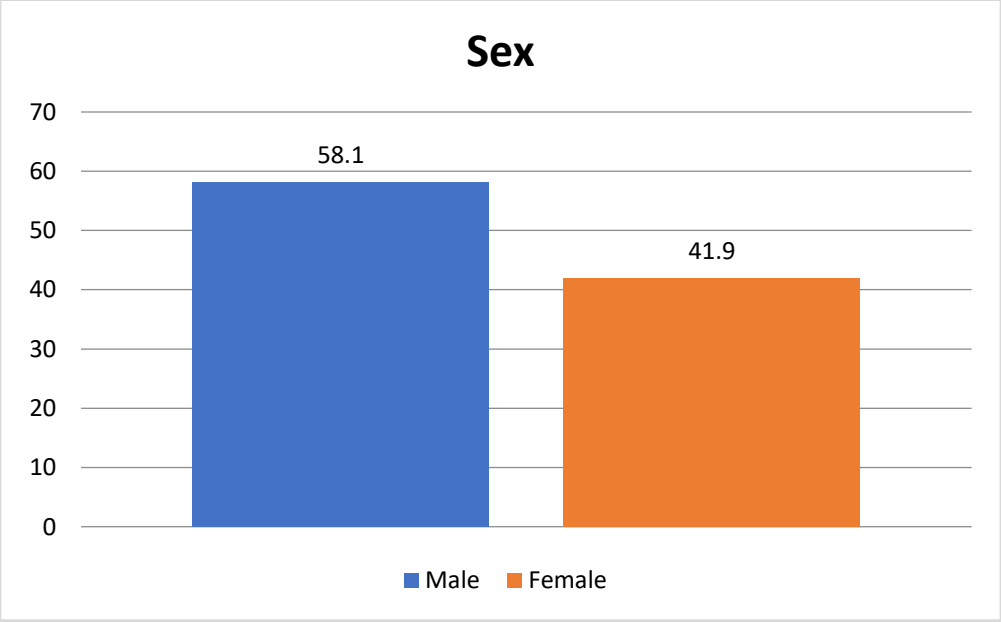

TABLE 3 AGE DISTRIBUTION

Age Group	No. of patients	% age of total patients
35 to 45	4	6.5
46 to 55	7	11.3
56 to 65	31	50.0
66 to 75	20	32.2
Total	62	100.0

From the above table and graph it was observed that majority of the patients that is 31 out of 62 patients (50.0%) were of the age group 56 to 65 years followed by 20 patients [32.2%] of the age group 66 to 75 years, 7 patients (11.3%) of the age group 46-55 years and 4 patients (6.5%) of the age group 35 to 45 years.

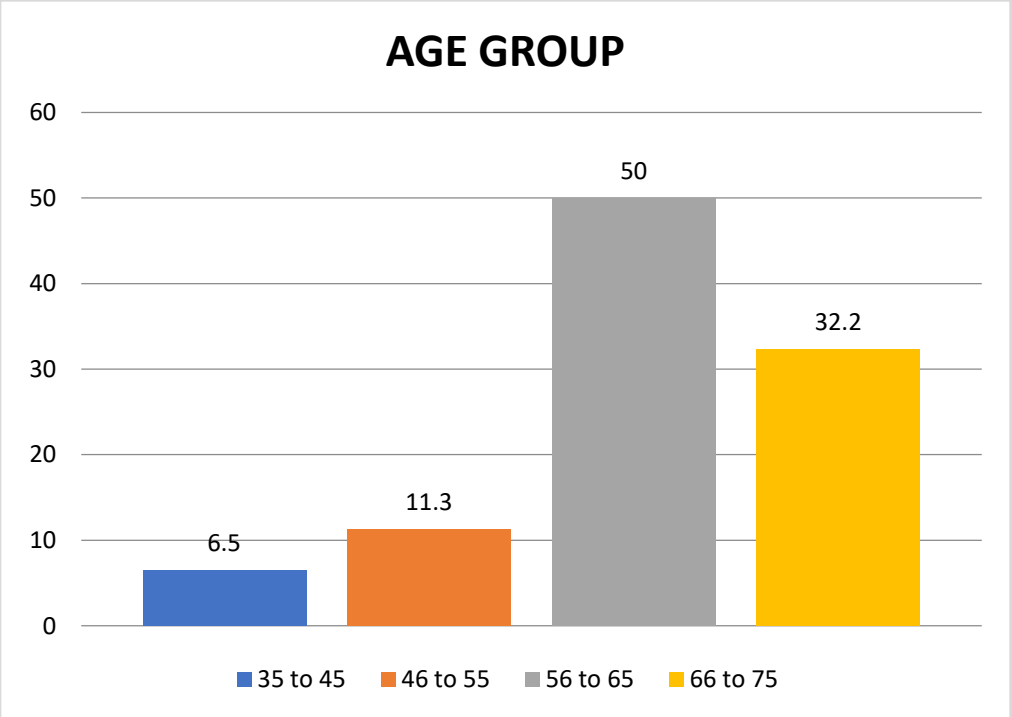

FIGURE 5 -AGE GROUP

TABLE 4 AGE DESCRIPTIVE

	N	Minimum	Maximum	Mean	Std. Deviation
Age	62	35.0	75.0	61.6	8.5

From the above table and graph it was observed that mean age of the patients was 61.6±8.5 years.

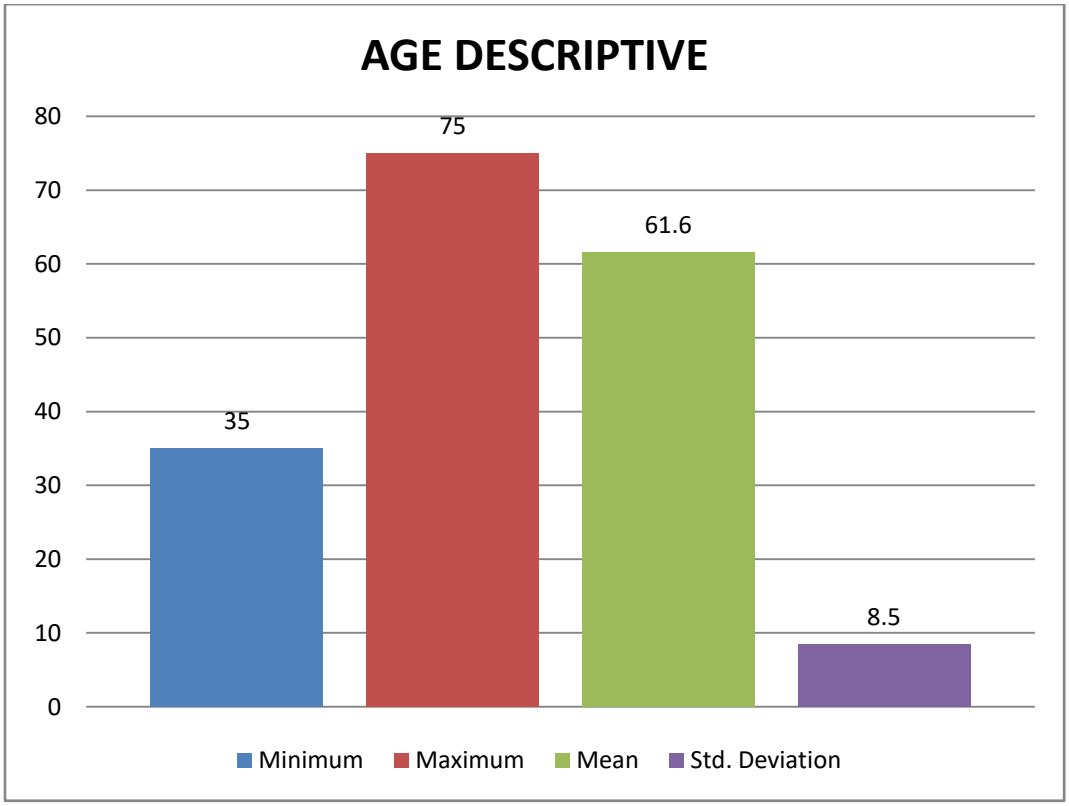

FIGURE 6- AGE DESCRIPTIVE

TABLE 5 - PRESENTING COMPLAINTS

Presenting Complaints And Duration	No. of patients	% age of total patients
Bony Pains	32	51.6%
Fractures	6	9.7%
Fatigue	48	77.4%
Dyspnea	19	30.7%
Weight Losss/Loss Of Appetite	33	53.2%
Decreased Urine Output	16	25.8%
Altered Sensorium	2	3.2%
Fever	26	41.9%

In our study, it was observed that most common presenting complaint was fatigue which was seen in 48 out of 62 patients (77.4%). Other predominant complaints were weight loss / loss of appetite which was seen in 33 out of 62 patients (53.2%), fever which was seen in 26 out of 62 patients (41.9%). Patients in our study also had other clinical presentations such as dyspnea which was seen in 19 out of 62 patients (30.6%), decreased urine output which was seen in 16 out of 62 patients (25.8%). Bone fractures were seen in 6 out of 62 patients (9.6%), altered sensorium which was seen in 2 out of 65 patients (3.2%). (Note-Some patients had more than one presenting complaint)

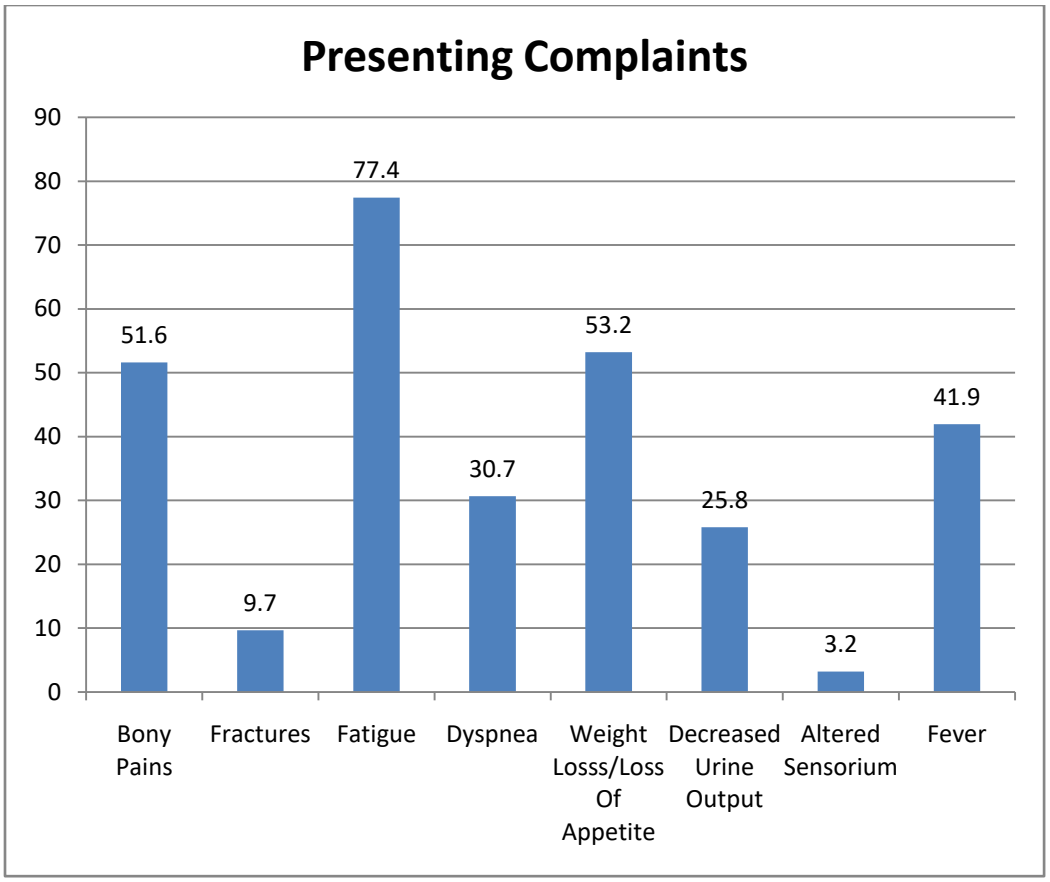

FIGURE 7 PRESENTING COMPLAINTS

TABLE 6 ANY OTHER COMPLAINTS

	No. of patients	% age of total patients
Burning Micturition	3	4.8
Cough	1	1.6
GI Bleed	2	3.2
Loose Stools	1	1.6

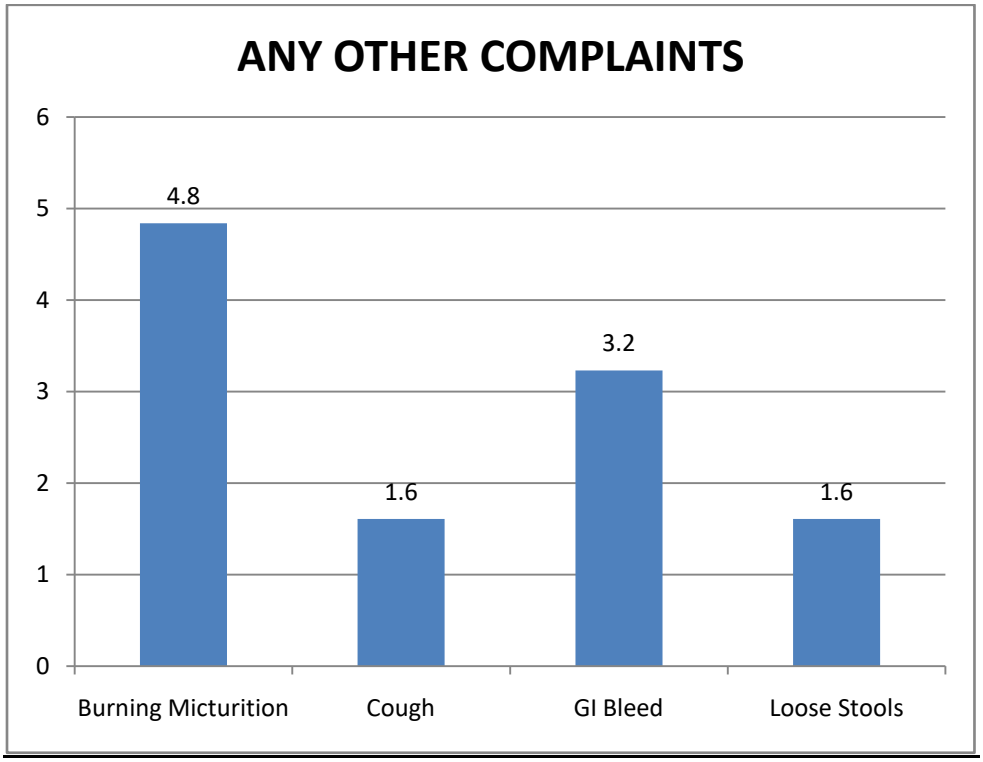

FIGURE 8 ANY OTHER COMPLAINTS

In our study, patients also had some rare presentations such as burning micturition which was seen by 3 patients (4.8%). 2 patients had GI bleed (3.2%), 1 patient had cough (1.6%) and 1 patient also presented with loose stools (1.6%).

TABLE 7 -COMORBIDITY

Comorbidity	No. of cases	Percentage
No	44	71.0%
CAD	2	3.2%
DM2	14	22.6%
HTN	11	17.7%

It was observed that out of 62 patients 14 were diabetic (22.6%), 11 were hypertensive(17.7%), and 2 patients had h/o coronary artery disease (3.2%).Out of 62, 2 patients had both diabetes mellitus type 2 and hypertension.

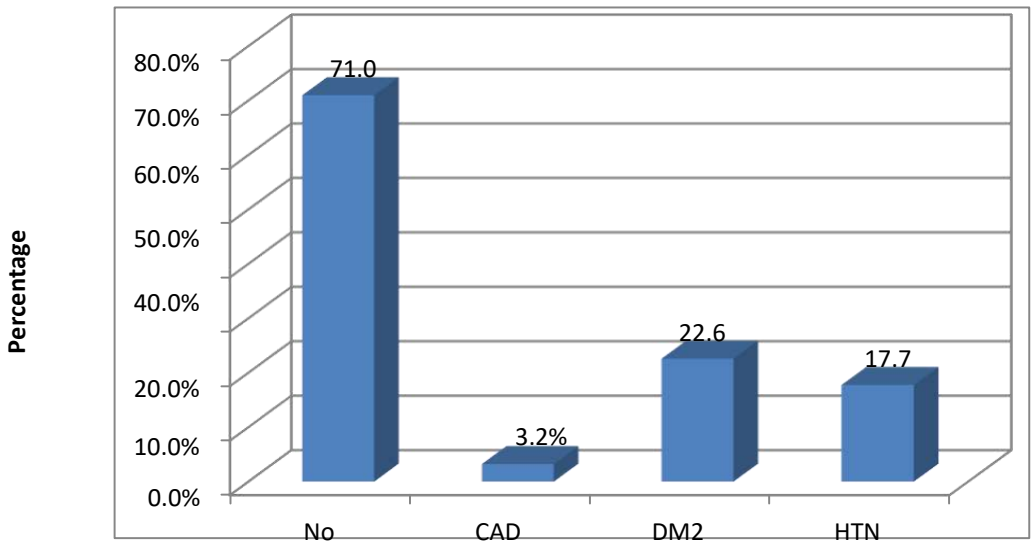

FIGURE 9- COMORBIDITY

TABLE 8- EXAMINATION

General Examination		
	No. of patients	**% age of total patients**
Pallor	50	80.6
Edema Feet	5	8.1
Icterus	0	0
SYSTEMIC EXAMINATION		
Hepatomegaly/Splenomegaly	-	-
Motor/Sensory Loss	-	-

In our study , the most common physical examination finding was pallor which was seen in 50 out of 62 patients (80.6%) followed by edema feet which was seen in 5 patients (8.1%). No patient out of 62 presented with hepatosplenomegaly, or icterus. No patient had any sensory or motor deficit on examination.

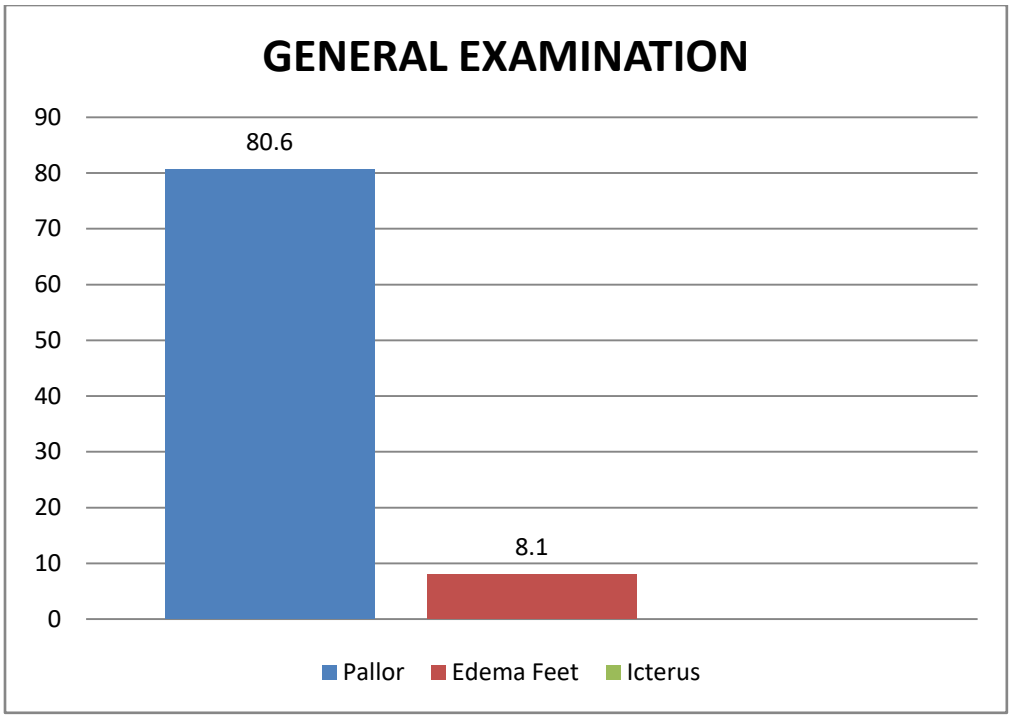

FIGURE 10- GENERAL EXAMINATION

TABLE 9 HEMOGLOBIN

Hemoglobin (gm/dl)		
Parameter	**No. of patients (n=62)**	**Percentage**
< 8	24	38.7%
8-10.0	22	35.5%
10-12.0	15	24.2%
> 12	1	1.6%
Total	62	100.0%

In our study, it was found that 24 out of 62 patients had Hb <8gm/dl (38.7%), 22 patients had Hb within 8-10gm/dl (35.5%), 15 out of 62 had Hb within 10-12gm/dl (24.2%), and only 1 patient had hb >12gm/dl (1.6%).

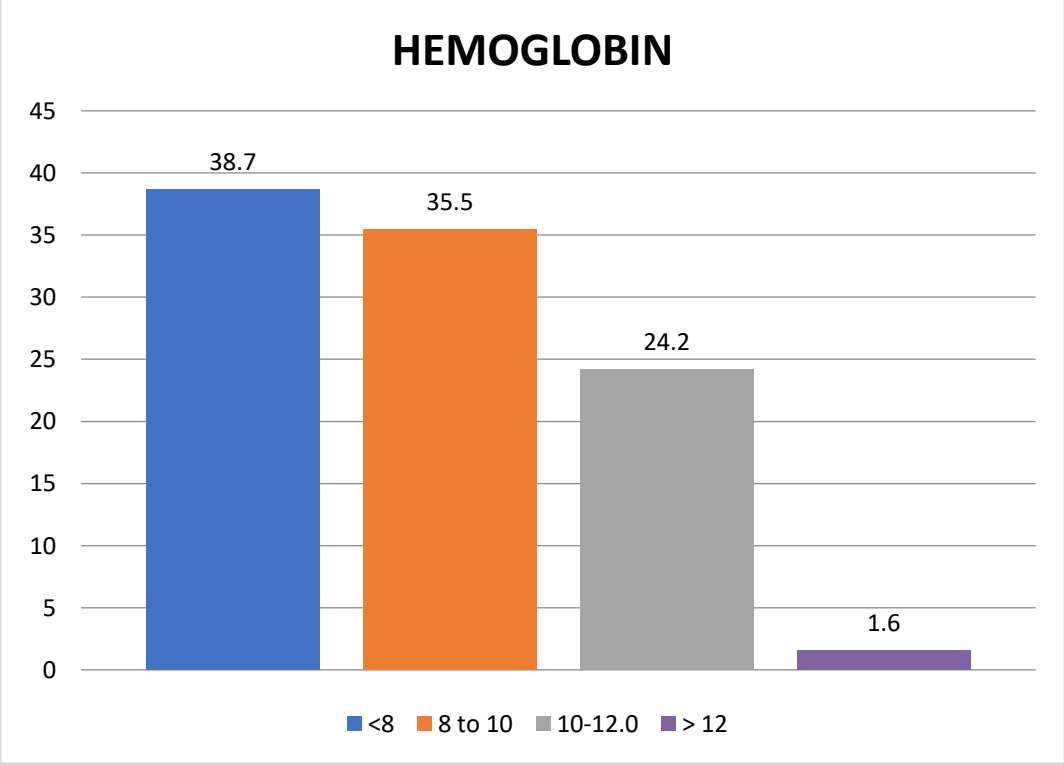

FIGURE 11- HEMOGLOBIN

TABLE 10 –PLATELET COUNT

Platelet Count(lakhs/mm3)		
Parameter (/mm3)	**No. of patients (n=62)**	**Percentage**
Less than 1.5 Lakh/mm3	16	25.8
More than 1.5 Lakh/mm3	46	74.2

In our study, it was found that 46 out of 62 patients had platelet count more than 1.5 lakh/mm3 (74.2%) and 16 patients had thrombocytopenia with platelet count less than 1.5 lakh/mm3 (25.8%).

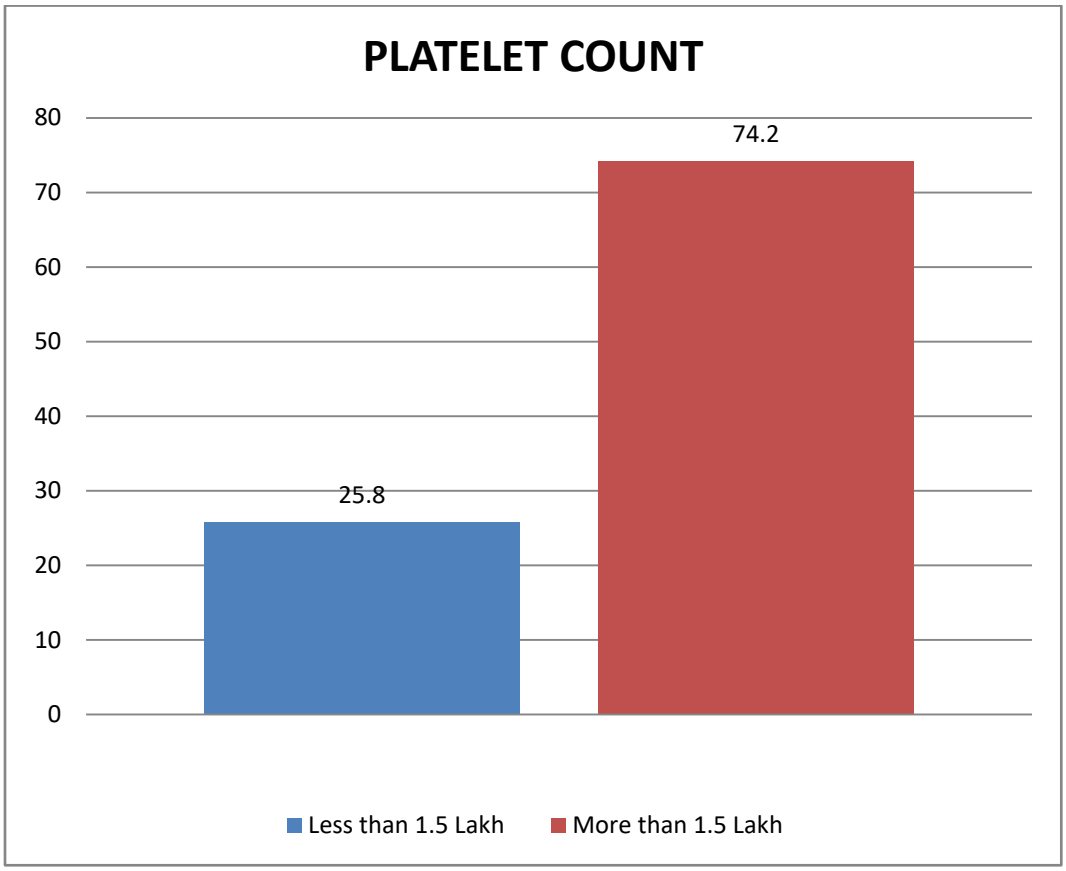

FIGURE 12- PLATELET COUNT

TABLE 11 TLC

TLC (10^3/mm3)	No. of cases	Percentage
< 4	7	11.3%
4-11	44	71.0%
> 11	11	17.7%
Total	62	100.0%

44 out of 62 patients had normal TLC count of 4-11 x$\mathbf{10^3}$/mm^3 (71%), 7 patients had leucopenia with TLC<4x10^3/mm^3 (11.3%) and 11 patients had leucocytosis with TLC >11x10^3/mm3 (17.7%).

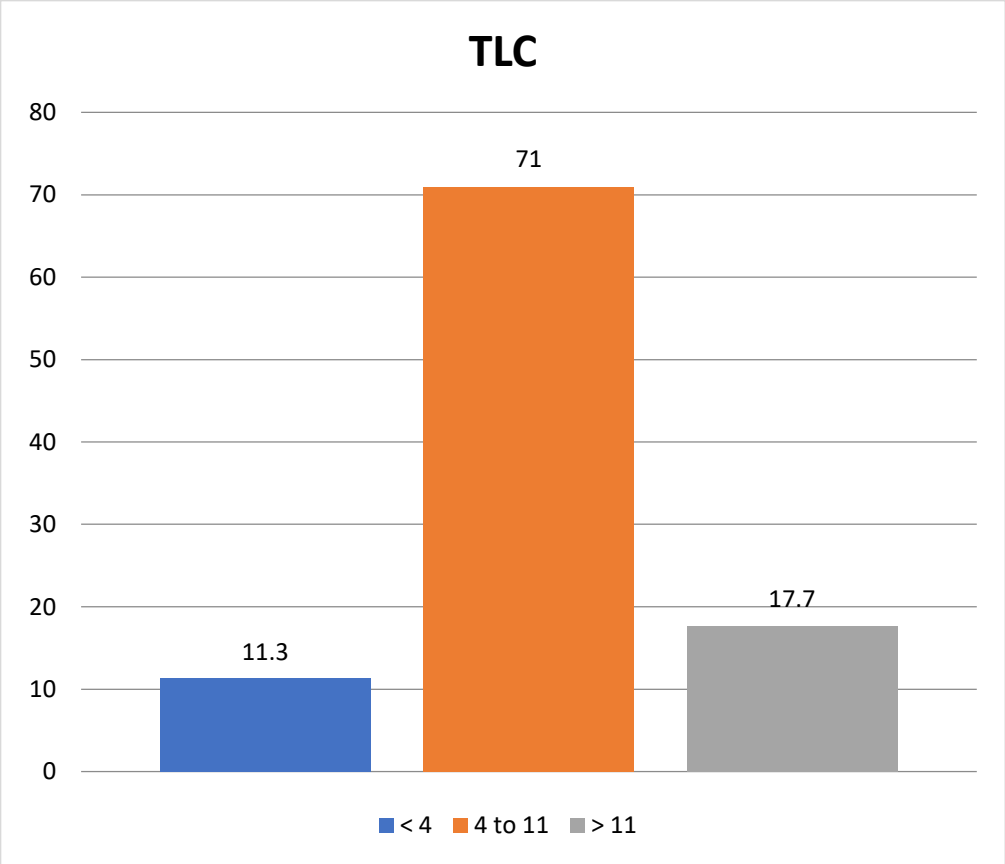

FIGURE 13- TLC

TABLE 12- ESTIMATED SEDIMENTATION RATE

ESR (mm/ hour)		
Parameter	**No. of patients (n=62)**	**Percent**
20 to 50	7	11.3
50 to 100	44	71.0
>100	11	17.7
Total	62	100.0

In our study, it was observed that majority of patients i.e 44 patients had ESR of 50-100 mm/hour (71.0%), 11 patients had elevated ESR of >100mm/hour (17.7%) and 7 patients had ESR within 20-50 mm/hour (11.3%). None of the patients had normal ESR.

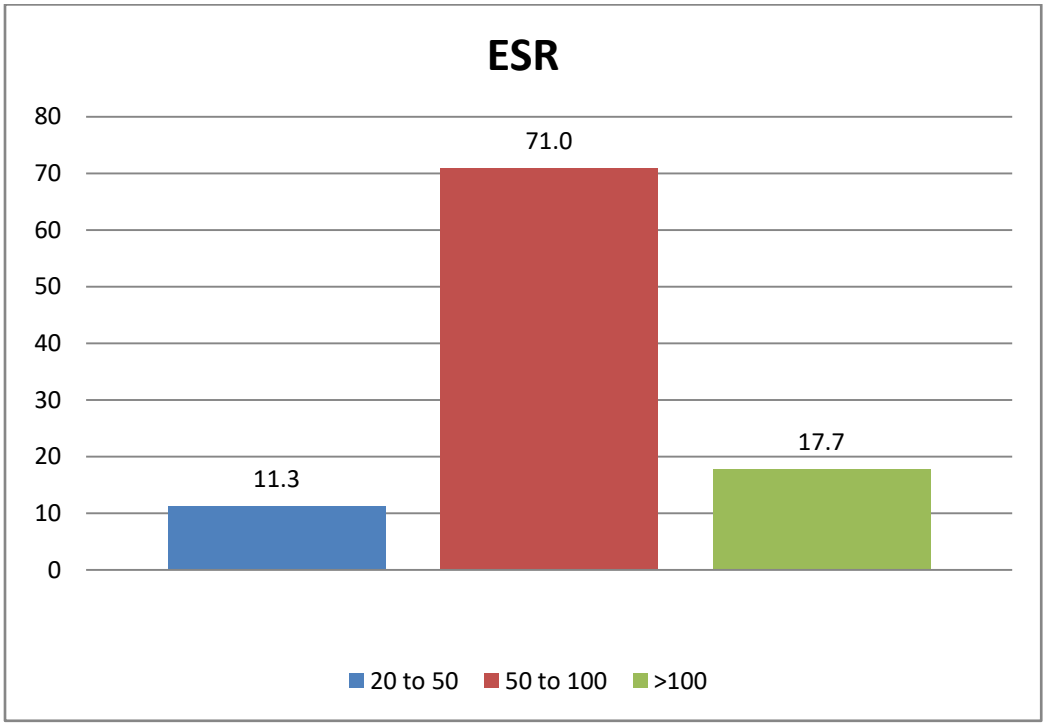

FIGURE 14 ESR

TABLE 13 PERIPHERAL BLOOD FILM

PBF	No. of cases	Percentage
RF-	24	38.70%
RF+	38	61.30%
Total	62	100.00%

On PBF, Rouleaux formation was seen in 38 out of 62 patients (61.3%) and it was absent of 24 out of 62 patients (37.1%).

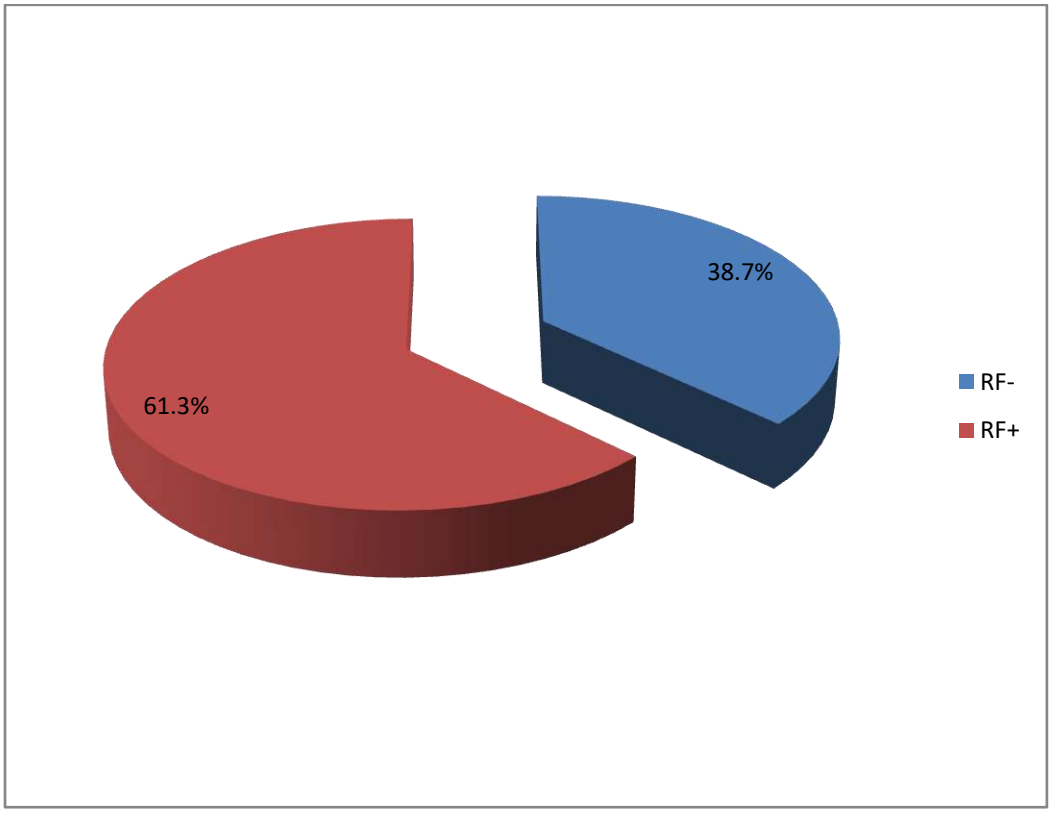

FIGURE 15 PERIPHERAL BLOOD FILM

TABLE 14 SERUM CREATININE

S.Creatinine [mg/dl]		
Parameter	**No. of patients (n=62)**	**Percentage**
<2	21	33.9
>2	41	66.1
Total	62	100.0

It was observed that majority of patients had serum creatinine >2 mg/dl i.e 41 out of 62 patients (66.1%) and 21 out of 62 patients had serum creatinine <2 mg/dl (33.9%)

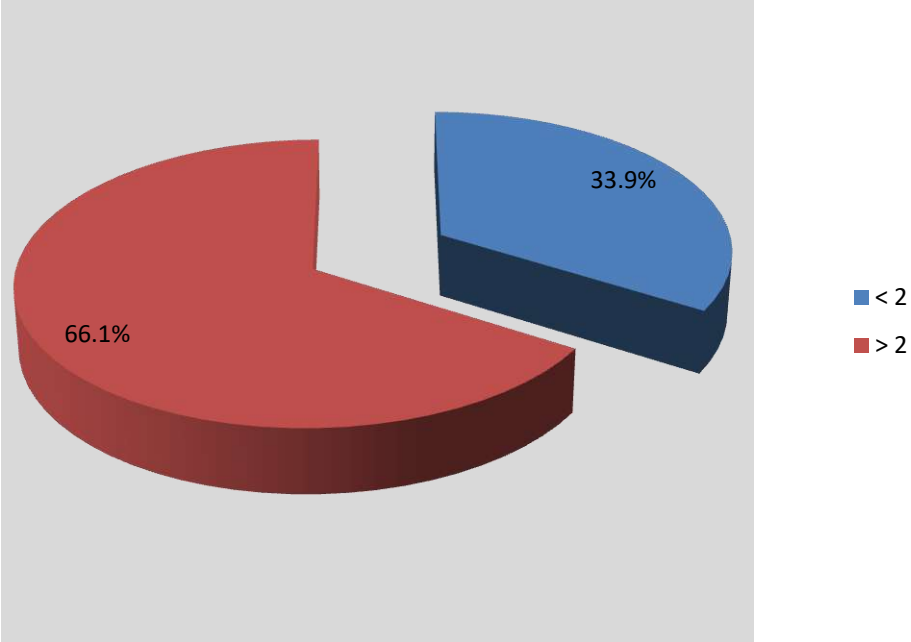

FIGURE 16 SERUM CREATININE

TABLE 15- SERUM BILIRUBIN

S.Bilirubin(mg/dl)		
Parameter	**No. of patients (n=62)**	**Percentage**
<1.2	59	95.2
>1.2	3	4.8
Total	62	100.0

In our study, majority of patients i.e 59 out of 62 patients (95.2%) had serum bilirubin of less than 1.2 mg/dl and 3 patients out of 62 patients had serum bilirubin of more than 1.2mg/dl (4.8%).

TABLE 16-SGOT

SGOT (U/L)		
Parameter	**No. of patients (n=62)**	**Percentage**
<40	23	37.0
>40	39	62.0
Total	62	100.0

39 out of 62 patients had elevated SGOT >40U/L (62%) and 23 patients (37%) had SGOT <40U/L.

TABLE 17-SGPT

SGPT (U/L)		
Parameter	**No. of patients (n=62)**	**Percentage**
<40	33	53.2
>40	29	46.8
Total	62	100.0

In our study, it was observed that 33 patients had SGPT<40 U/L (53.2%) and 29 patients (46.8%) had SGPT>40U/L.

TABLE 18- ALKALINE PHOSPHATASE

Alkaline Phosphatase (IU/L)		
Parameter	**No. of patients (n=62)**	**Percentage**
<129	54	87.1
>129	8	12.9
Total	62	100.0

In our study, it was observed that majority of the patients i.e 54 patients (87.1%) had Alkaline Phosphate<129 IU/L and 8 patients (12.9%) had Alkaline phosphate >129IU/L

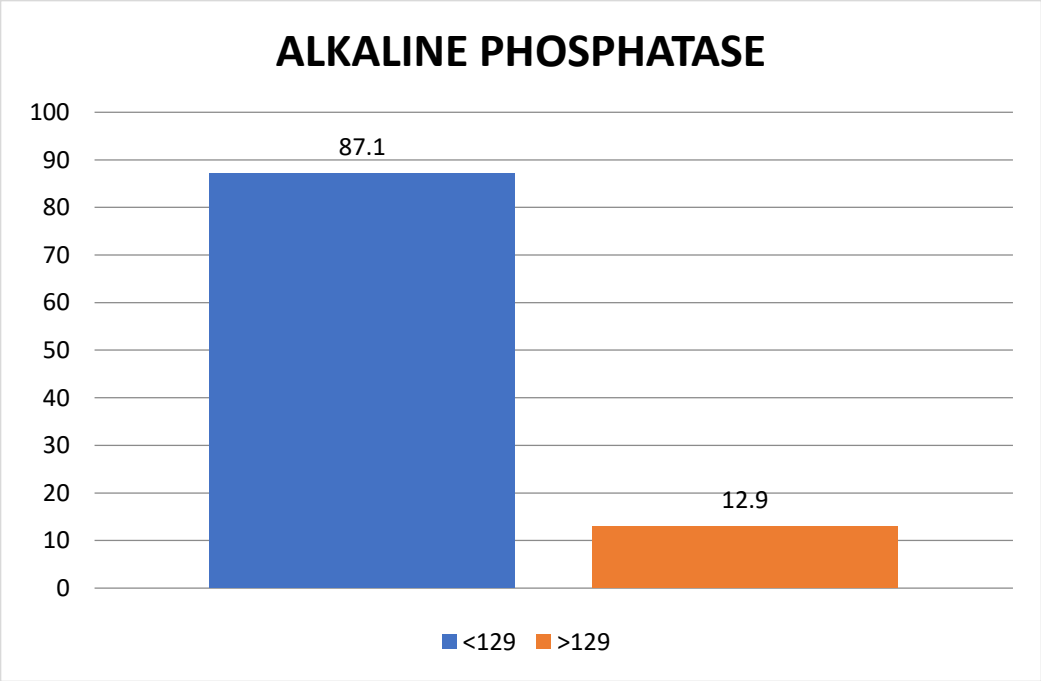

FIGURE 17- ALKALINE PHOSPHATASE

TABLE 19 CORRECTED CALCIUM

Corrected Calcium (mg/dl)		
Parameter	**No. of patients (n=62)**	**Percentage**
8.5 to 10.2	1	1.6
10.3 to 11	8	12.9
>11	53	85.5
Total	62	100.0

According to IMWG criteria of multiple myeloma, hypercalcemia is defined as calcium levelsof >11mg/dl. So, in our study 53 out of 62 patients (85.5%) had hypercalcemia , 8 out of 62 patients (12.9%) had calcium levels between 10.3-11.0mg/dl, and 1 patient (1.6%) had calcium levels between 8.5-10.2mg/dl.

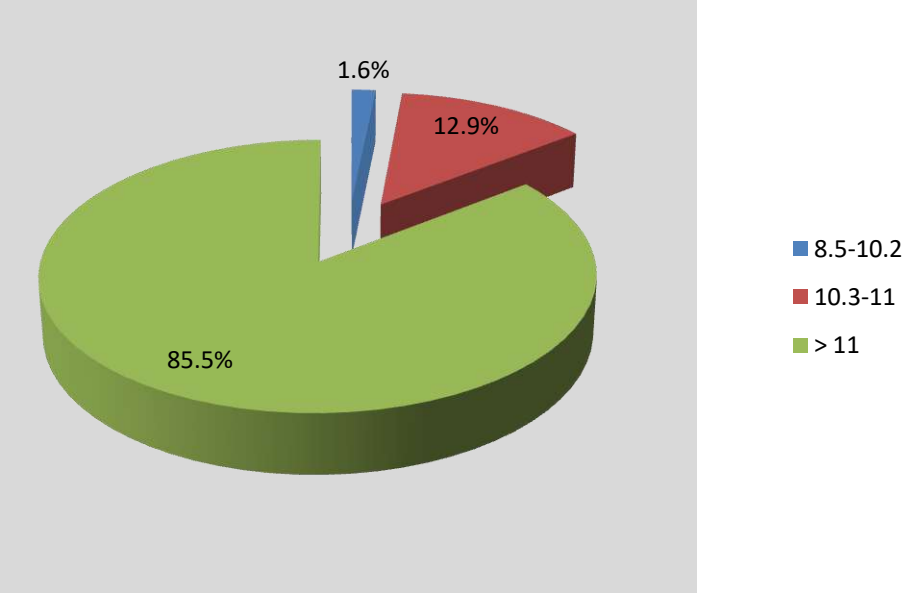

FIGURE 18 CORRECTED CALCIUM

TABLE 20 SERUM ALBUMIN

Serum Albumin (gm/dl)		
Parameter	**No. of patients (n=62)**	**Percentage**
<3.5	35	56.5
>3.5	27	43.5
Total	62	100.0

In our study, it was observed that the majority of the patients 56.5% had Serum Albumin <3.5 gm/dl and 43.5% had Serum Albumin > 3.5 gm/dl.

TABLE 21 SERUM TOTAL PROTEINS

Serum Total Protein(gm/dl)		
Parameter	**No. of patients (n=62)**	**Percentage**
4 to 6	10	16.1
6 to 9	44	71.0
>9	8	12.90
Total	62	100.0

In our study, it was observed that 44 out of 62 patients (71.0%) had serum total proteins from 6 to 9 gm/dl and 10 out of 62 patients (16.1%) had total serum albumin from 4 to 6 gm/dl and 8 patients out of 62 had serum total proteins of >9gm/dl (12.9%).

TABLE 22 GLOBULIN (gm/dl)

Globulin (gm/dl)		
Parameter	**No. of patients (n=62)**	**Percentage**
< 2.0	2	3.20
2-3.5	15	24.20
> 3.5	45	72.60
Total	62	100.00

Out of 62 patients, 45 patients had increased serum globulins >3.5gm/dl, 15 patients had normal globulins (2-3.5gm/dl), 2 patients had low levels of serum globulins (<2gm/dl).

TABLE 23 A/G RATIO

Parameter	No. of patients (n=62)	Percentage
< 1.1	51	82.30
1.1-2.5	10	16.10
> 2.5	1	1.60
Total	62	100.00

Out of 62 patients 51 patients had a/g ratio reversal i.e <1.1(82.3%), 10 patients had normal ratio 1.1-2.5(16.1%), whereas 1 patient had ratio >2.5(1.6%).

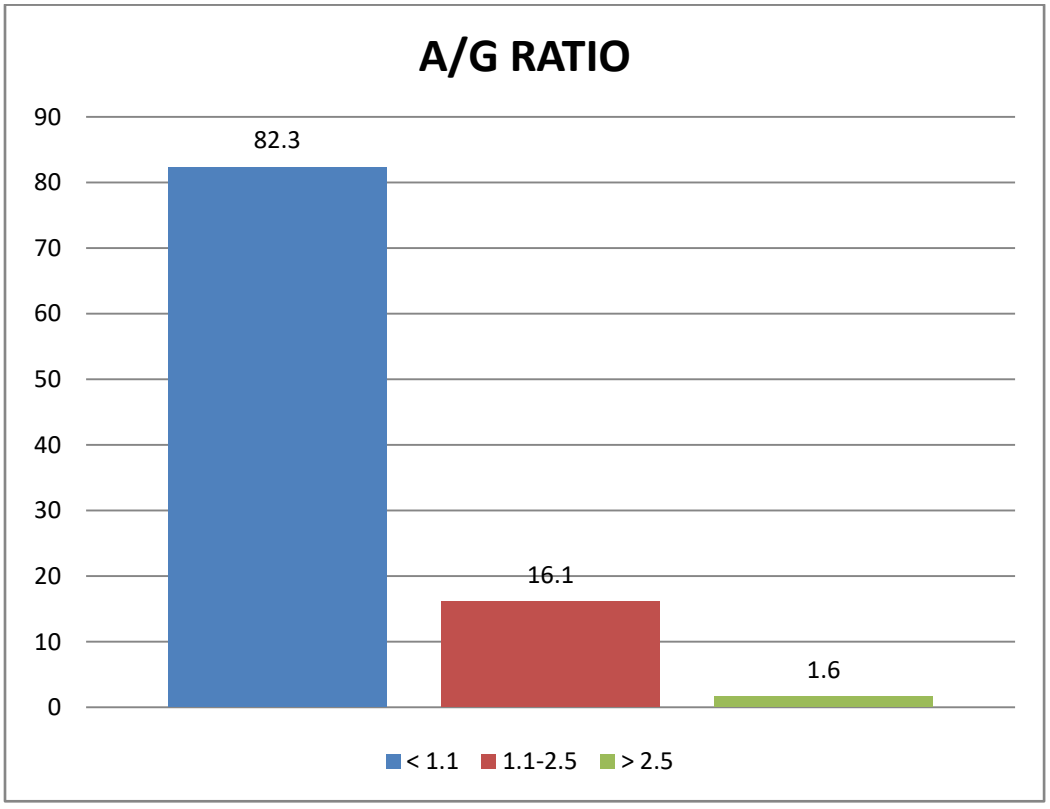

FIGURE 19- A/G RATIO

TABLE 24 - BETA 2 MICROGLOBULIN (mg/l)

Parameter	No. of patients (n=62)	Percentage
<3.5	13	21.0
>3.5	49	79.0
Total	62	100.0

In our study, it was observed that majority of the patients 49 out of 62 patients (79.0%) had Beta 2 microglobin <3.5 mg/l and 13 patients out of 62 (21%) had Beta 2 microglobin <3.5 mg/l.

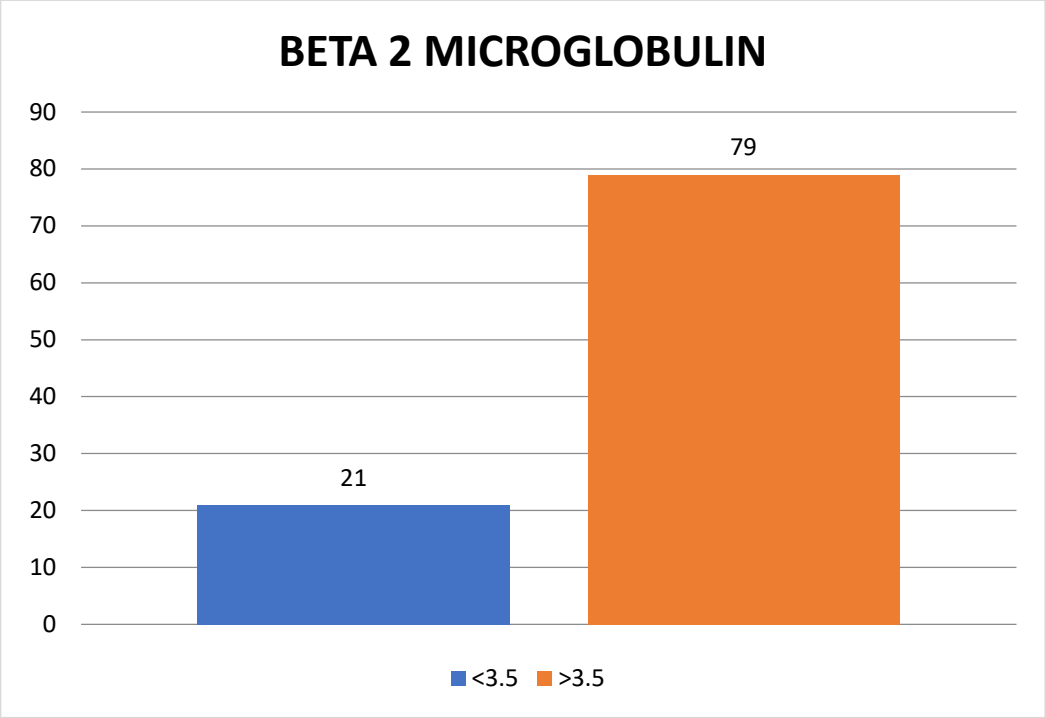

FIGURE 20 BETA 2 MICROGLOBULIN

TABLE 25- BETA 2 MICROGLOBULIN DESCRIPTIVE

in mg/l	N	Minimum	Maximum	Mean	Std. Deviation
Beta 2 microglobulin	62	1.4	26.4	7.2	5.3

In our study, the mean Beta-2 microglobulin levels were found to be 7.2 ± 5.3 mg/l.

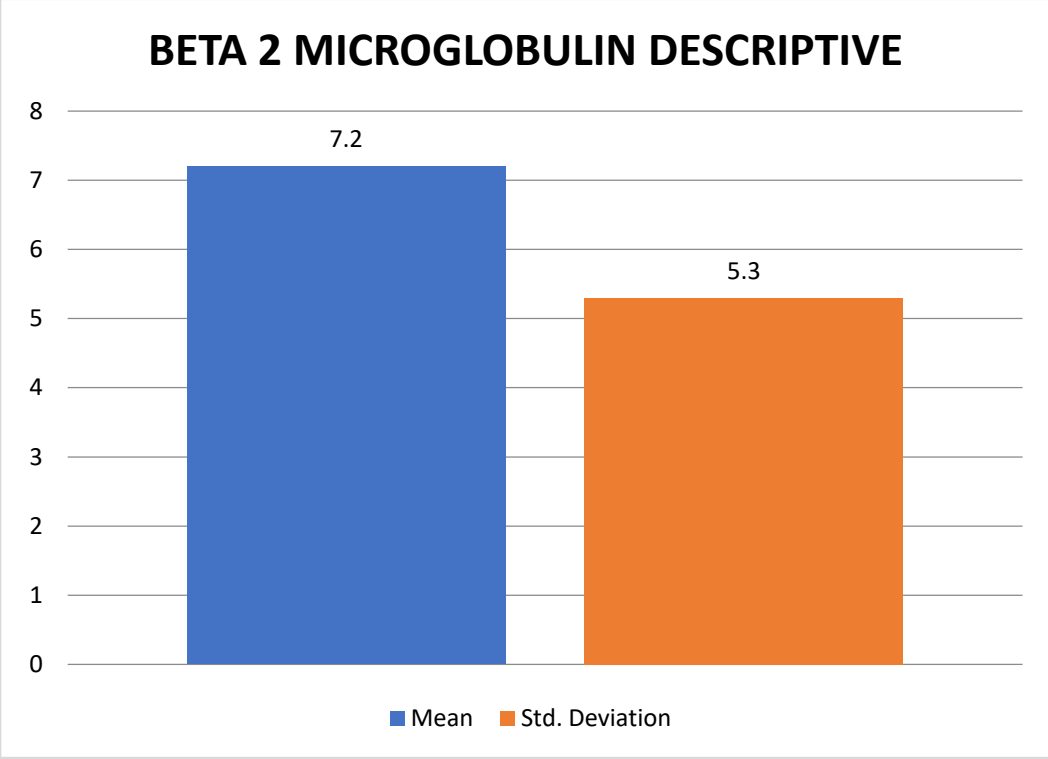

FIGURE 21- BETA 2 MICROGLOBULIN DESCRIPTIVE

TABLE 26 SERUM LDH

Serum LDH(IU/L)		
Parameter	**No. of patients (n=62)**	**Percentage**
<225	20	32.3
>225	42	67.7
Total	62	100.0

In our study, majority of the patients i.e 42 out of 62 patients (67.7%) had Serum LDH >225 mg/dl and 20 out of 62 patients [32.3%] had Serum LDH <225 mg/dl.

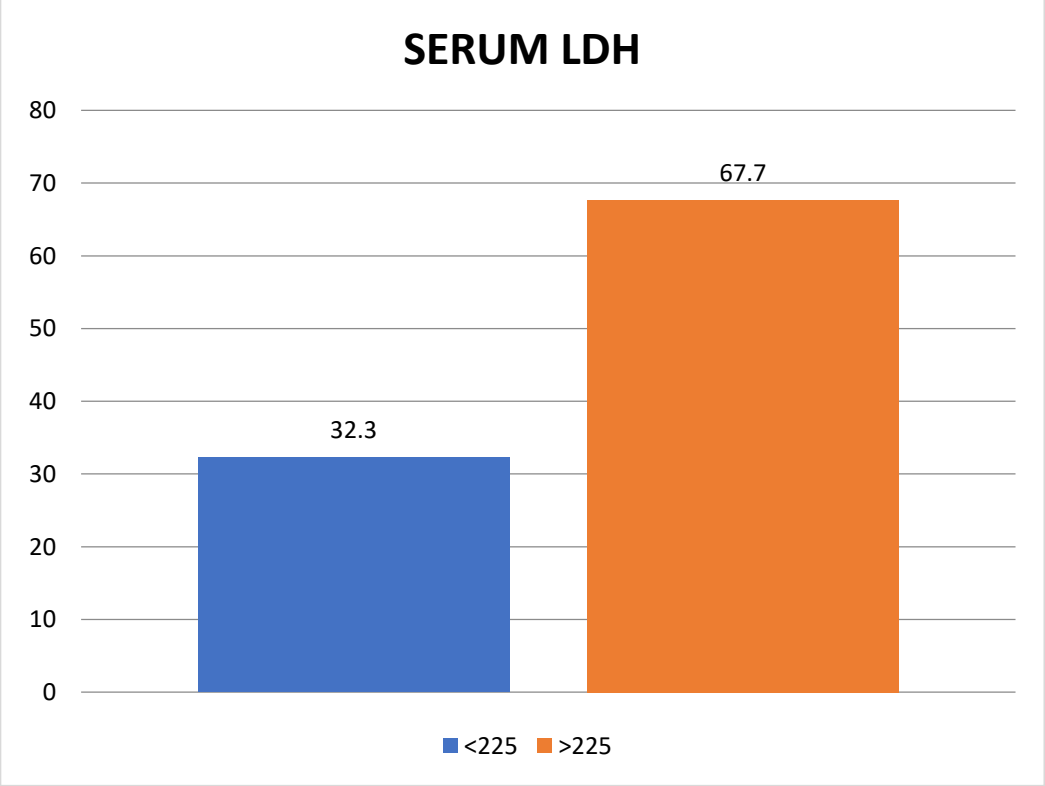

FIGURE 22 – SERUM LDH

TABLE 27- SERUM PROTEIN ELECTROPHORESIS

Serum Protein Electrophoresis		
	No. of patients	**% age of total patients**
M SPIKE +	58	93.5
M SPIKE -	04	6.5
Total	62	100.0

Majority of the patients 58 out of 62 patients (93.5%) had Serum Protein Electrophoresis M Spike + and 04 patients [6.5 %] had no M spike seen.

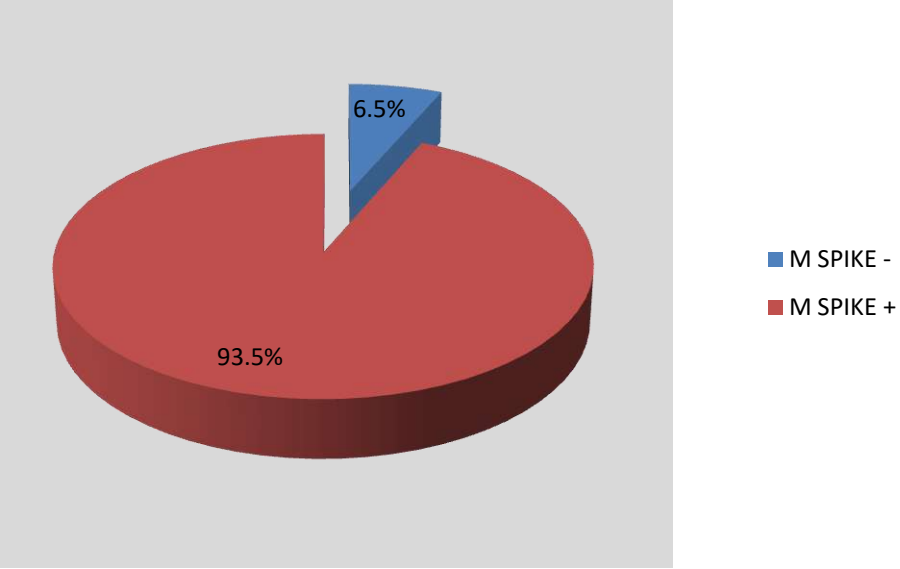

FIGURE 23- SERUM PROTEIN ELECTROPHORESIS

TABLE 28 SERUM IMMUNOFIXATION

Serum Immunofixation	No. of cases	Percentage
IgA KAPPA MONOCLONAL GAMMOPATHY	13	21.0%
IgA LAMBDA MONOCLONAL GAMMOPATHY	1	1.6%
IgG LAMBDA MONOCLONAL GAMMOPATHY	20	32.3%
IgG KAPPA MONOCLONAL GAMMOPATHY	27	43.5%
NORMAL	1	1.6%
Total	62	100.0%

On serum immunofixation, 13 out of 62 patients had IgA kappa monoclonal gammopathy (21.0%), 1 patient had IgA lambda monoclonal gammopathy (1.6%), 20 patients had IgG lambda monoclonal gammopathy (32.3%), 27 patients had IgG kappa monoclonal gammopathy (43.5%), and 1 patient had normal immunofixation (1.6%).

TABLE 29 MEAN OF VARIABLES

	N	Minimum	Maximum	Mean	Std. Deviation
Age	62	35.0	75.0	61.6	8.5
BMI	62	19.0	31.0	25.6	2.6
HB	62	4.0	12.2	8.5	2.0
Platelet count	62	34000.0	550000.0	192258.1	83711.8
ESR	62	28.0	144.0	78.6	24.1
TLC	62	1.1	44.0	8.6	5.8
S.Creatinine	62	0.6	9.8	2.9	1.7
S.Bilirubin	62	0.1	2.1	0.4	0.4
SGOT	62	15.0	90.0	44.0	20.4
SGPT	62	11.0	186.0	41.6	30.0
Alkaline Phosphatase	62	46.0	450.0	108.9	91.0
CORRECTED CALCIUM	62	10.2	16.8	12.6	1.4
Serum Albumin	62	1.8	3.8	3.0	0.6
Serum Total Protein	62	4.9	9.6	7.6	1.3
Serum LDH	62	106.0	826.0	394.0	199.8
K/L	13	0.0	1704.0	192.1	464.5
FREE K	13	2.5	13189.0	1296.3	3628.6
FREE-L	13	1.1	22745.0	1808.6	6291.3
GLOBULIN	62	1.2	7.3	4.6	1.4
A/G RATIO	62	0.2	3.0	0.8	0.5
Beta 2 microglobulin	62	1.4	26.4	7.2	5.3

It was found that in our study the mean Hb was found to be 8.5gm/dl , mean platelet counts was found to be 192258.1 / mm3 , mean ESR was found to be 78.6 mm/hour , mean TLC was found to be 8.6x $10^3/mm^3$, mean creatinine was found to be 2.9mg/dl, mean bilirubin was found to be 0.4 mg/dl, mean SGOT and SGPT was found to be 44 U/L and 41.6 U/L, mean ALP was found to be 81.1 IU/L, mean corrected calcium in our study was found to be 12.6 mg/dl, mean serum albumin was found to be 3.0 gm/dl, mean total serum protein was found to be 1.3 gm/dl, mean serum globulin was found to be 4.6gm/dl, mean A/G ratio was 0.8, mean serum LDH in our study was found to be 394.0 IU/L. Mean free kappa chain was found to be 1296.3 gm/dl, mean free lambda chain was found to be 1808.6 gm/dl. Mean K/L chain in our study was found to be 192.1. Mean beta 2 microglobulin was 7.2mg/l.

TABLE 30 Bone Marrow Aspirate / Biopsy

Bone Marrow Aspirate / Biopsy	No. of cases	Percentage
NORMAL	3	4.80%
PLASMA CELL DYSCRASIA	58	93.50%
PLASMA CELL PROMINENCE	1	1.60%
Total	62	100.00%

On bone marrow examination, 58 out of 62 patients had plasma cell dyscrasias (93.6%), 1 patient had plasma cell prominence (1.6%) and 3 patients had normal marrow (4.8%). Plasma cell dyscrasia seen in 58 out of 62 patients (93.6%) included plasma cells of 10% or more with or without plasmablastic morphology and plasma cells >30% were seen 24 out of 62 patients (38.7%).

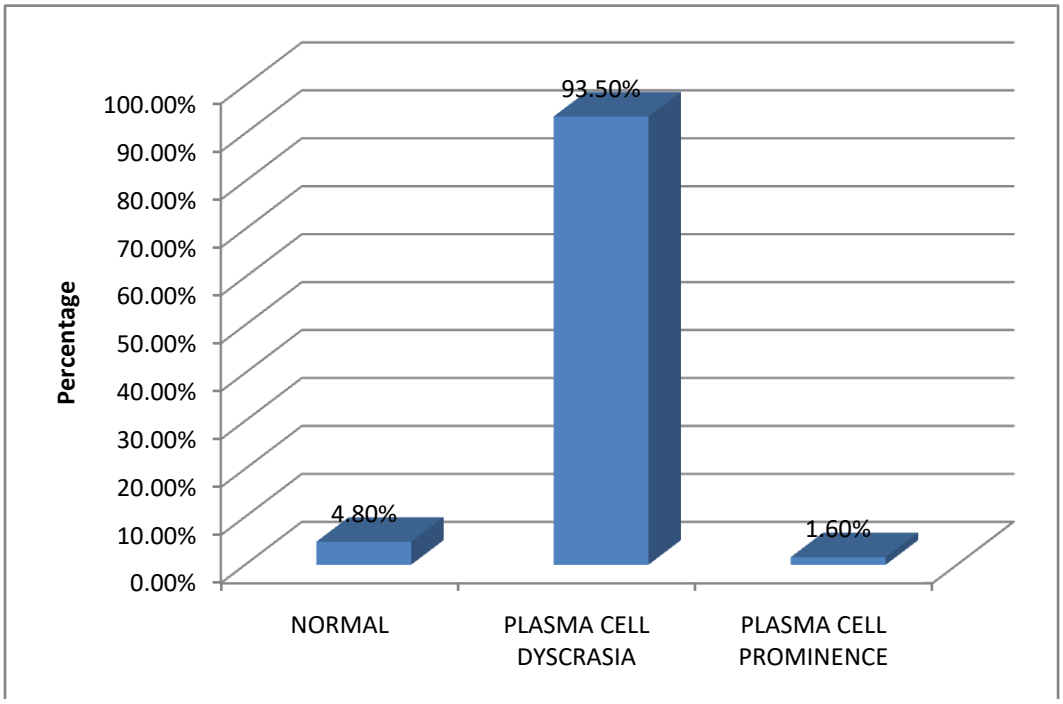

FIGURE 24- BONE MARROW ASPIRATE/BIOPSY

TABLE 31 SKELETAL SURVEY/ PET-CT SCAN FINDINGS

Skeletal Survey/ PET-CT Scan	No. of cases	Percentage
# L2 VERTEBRA	1	1.6%
# L2-L3 VERTEBRAE	1	1.6%
# L4 -L5 VERTEBRAE	1	1.6%
# L4 VERTEBRAE	1	1.6%
# LEFT ANT RIBS	1	1.6%
# RIBS LEFT SIDE	1	1.6%
# VERTEBRAE L3-L4	1	1.6%
BONY LYTIC LESION	37	59.7%
D4-D6 WEDGE COLLAPSE	1	1.6%
D8 # AND D8-D10 COLLAPSE	1	1.6%
D8-9 COLLAPSE	1	1.6%
DIFFUSE OSTEOPENIA	7	11.3%
PARTIAL COLLAPSE D3, D8-D10	1	1.6%%
NORMAL	7	11.3%%
Total	62	100.0%

It was observed in our study that majority of patients i.e 37 out of 62 patients had bony lytic lesions (59.7%), 7 out of 62 patients had normal skeletal survey (11.3%), 7 out of 62 patients had diffuse osteopenias (11.3%), 8 out of 62 patients had different types of fractures on skeletal survey (12.9%), rest of them had rare presentations such as vertebral collapse and diffuse vertebral myeloma lesions.

TABLE 32 MOLECULAR PROFILE

Molecular Profile		
t [4:14]	10	16.1
t [11:14]	13	21.0
t [14:16]	7	11.3
p53 del [17p13del]	3	4.9
negative	29	46.7
Total	62	100.0

In our study, majority of the patients i.e 13 out of 62 patients (21.0%) had Molecular Profile- t[11:14] positive and 10 patients had t[4:14] [16.1%] , 7 patients had t[14:16] positive (11.3%), 3 patients had p53 del+ (4.9%). Rest of the patients (29 out of 62 patients) had negative molecular profile (46.7%)

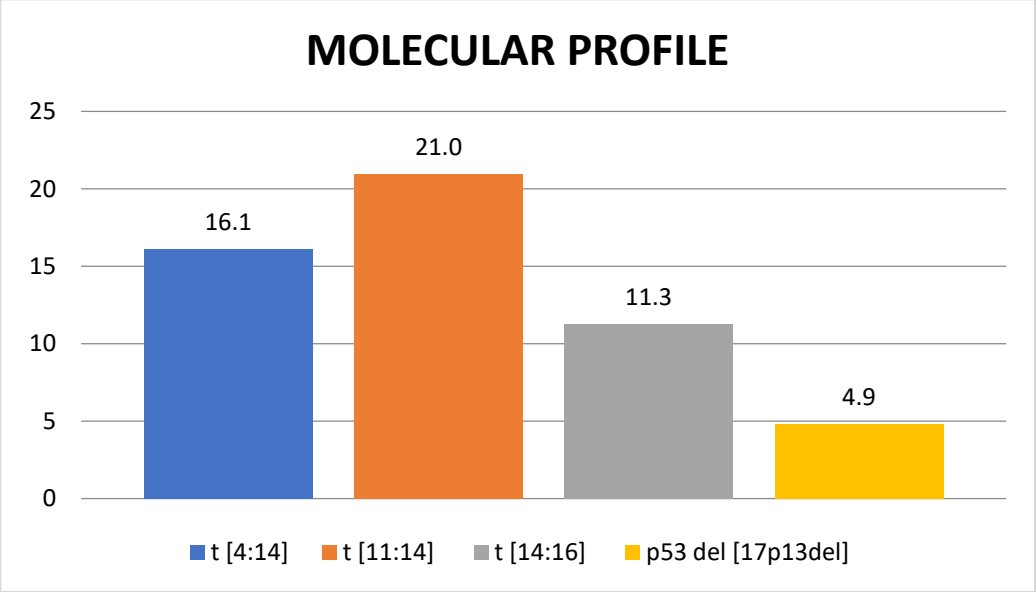

FIGURE 25 MOLECULAR PROFILE

TABLE 33 STAGING OF MULTIPLE MYELOMA

Stage	Frequency	Percentage
Stage I	0	0.00
Stage II	28	45.2
Stage III	34	54.8
Total	62	100.0

In our study, it was observed that majority of the patients i.e 34 out of 62 patients (54.8%) in our study had stage III of multiple myeloma and 28 out of 62 patients [45.2%] had stage II of multiple myeloma. No patient was reported to have stage I of Multiple myeloma in our study.

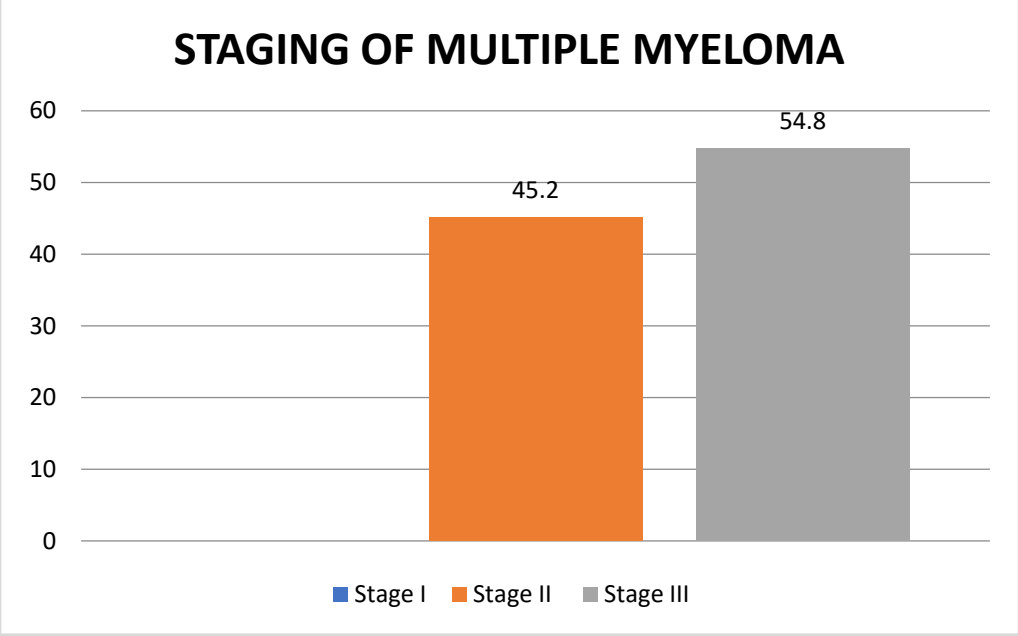

FIGURE 26- STAGING OF MULTIPLE MYELOMA

TABLE 34 TREATMENT

Treatment	Frequency	Percentage
Indoor	56	90.3
Outdoor	6	9.7
TOTAL	62	100.0

Majority of the patients in our study that is 56 out of 62 patients (90.31%) were admitted and started on treatment as indoor patients and 6 out of 62 patients [9.68%] out of all patients were treated on OPD basis.

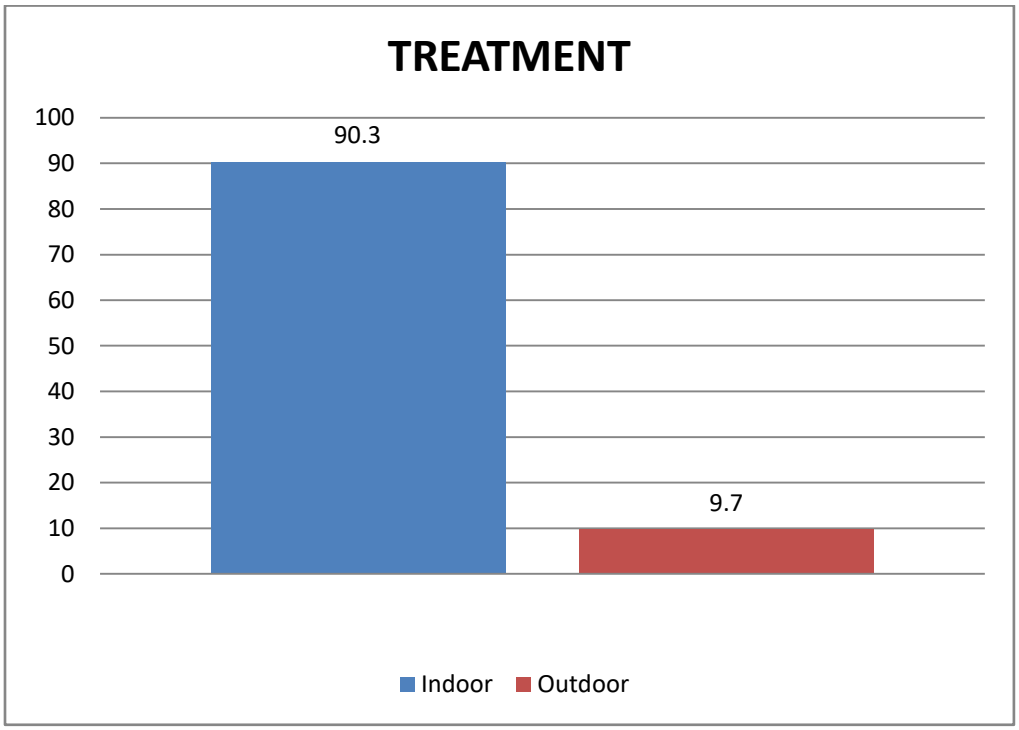

FIGURE 27- TREATMENT

TABLE 35- TREATMENT REGIMENS

Treatment	Frequency	Percentage
Bortezomib, Dexamethasone and Lenalidomide Regimen	26	41.9
Bortezomib, Dexamethasone and Cyclophosphamide Regimen	14	22.6
Bortezomib, Dexamethasone and Thalidomide Regimen	11	17.8
Dexamethasone and Bortezomib Regimen	8	12.9
Dexamethasone and Thalidomide	3	4.8
Total	62	100.0

All the 62 patients were started on treatment, 26 patients out of 62 (41.9%) were treated with Lenalidomide, Dexamethasone and Bortezomib regimen followed by 14 patients (22.6%) who were treated with Cyclophosphamide, Dexamethasone and Bortezomib Regimen, 11 patients (17.8%) were treated with Bortezomib, Dexamethasone and Thalidomide regimen, 8 patients (12.9 %) were treated with Bortezomib and Dexamethasone regimen , 3 patients (4.8%) patients were treated with Dexamethasone and Thalidomide regimen.

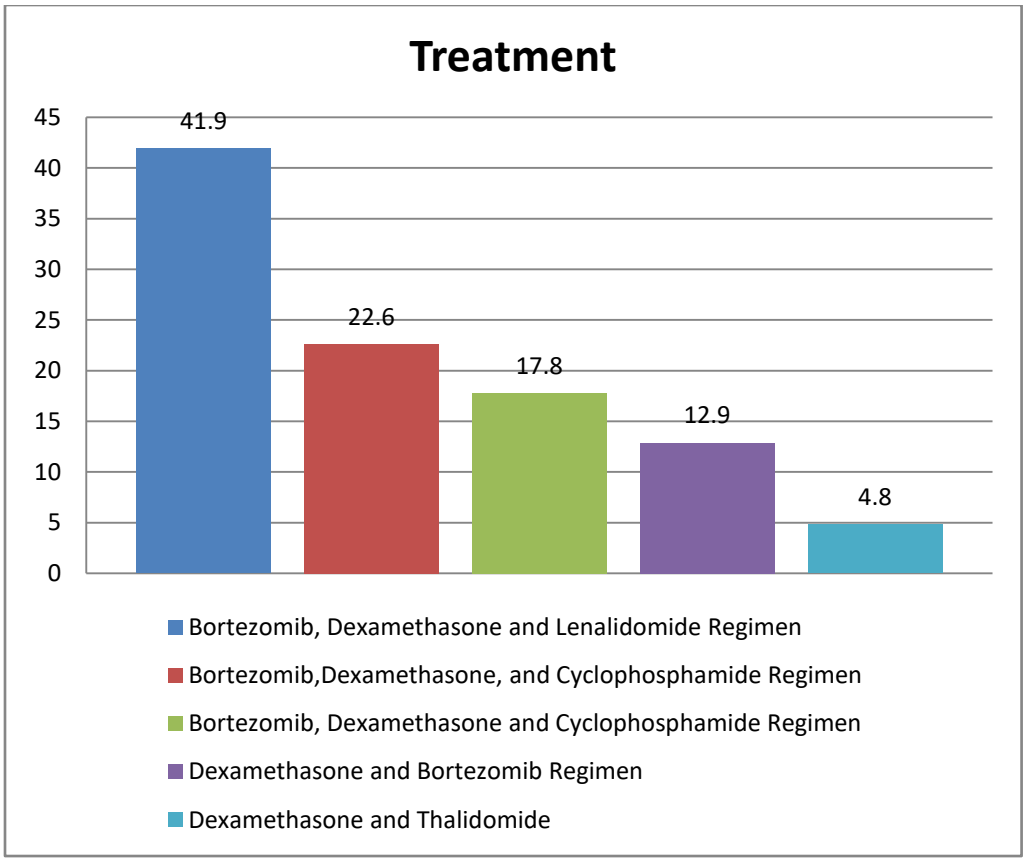

FIGURE 28 TREATMENT REGIMENS

TABLE 36 OUTCOME

Stage	Frequency	Percentage
Death	3	4.8%
Discharge /DAMA	59	95.2%

In our study, it was observed that majority of the patients that is 59 out of 62 patients (95.2 %) got discharged or took discharge against medical advice **(DAMA)** while 3 patients (4.8%) got expired.

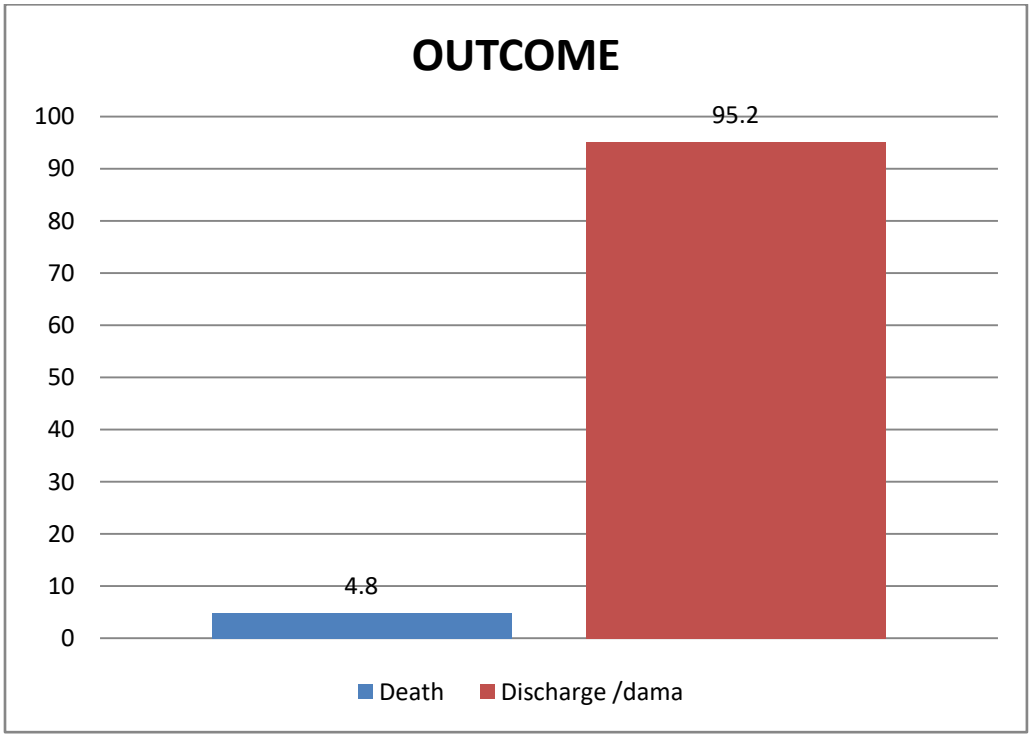

FIGURE 29 OUTCOME

The parameters like age, sex, serum creatinine, serum albumin etc. were compared between the stage II and stage III groups.

TABLE 37 STAGE TO SEX

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
	Male	16	57.1%	20	58.8%	36		
Sex	Female	12	42.9%	14	41.2%	26	0.018	0.894
Total		28	100.0%	34	100.0%	62		

In our study , it was observed that 16 out of 28 people in stage II were males (57.1%) and 20 out of 34 patients in stage III were male (58.8%). Out of 28 patients in stage II, 12 were female (42.9%) and out of 34 patients in stage III, 14 were female (41.2%).

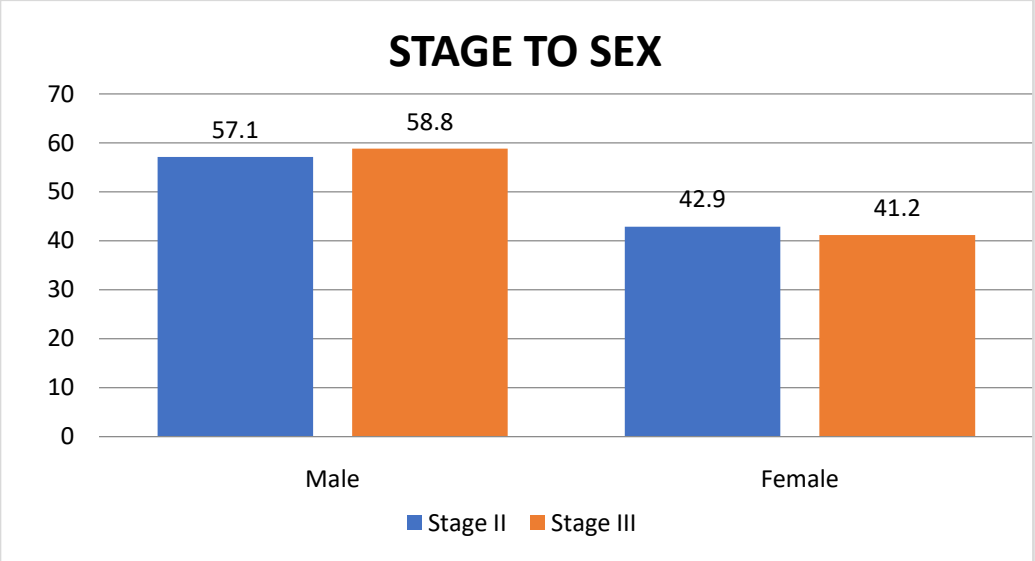

FIGURE 30- STAGE TO SEX CORRELATION

TABLE 38 STAGE TO AGE

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
AGE	**35 to 45**	3	10.7%	1	2.9%	4	0.422	0.113
	46 to 55	3	10.7%	4	11.8%	7		
	56 to 65	13	46.4%	18	52.9%	31		
	66 to 75	9	32.1%	11	32.4%	20		
	Total	28	100.0 %	34	100.0 %	62		

Our study concluded that:

3 patients out of 28 patients in stage II were from age group 35-45 years (10.7%) and only 1 patient out of total 34 patients in stage III was from age group 35-45 years (2.9%).

Similarly, 3 patients out of 28 patients in stage II were from age group 46-55 years (10.7%) whereas 4 patients out of 34 patients in stage III were from the same age group 46-55 years.

13 (majority of patients in stage II) out of 28 patients (46.4%) were from the age group 56-65 years and majority of patients in stage III (18 out of 34 patients) were also from the same age group.

9 patients out of 28 patients of stage II were from age group 66-75 years (32.1%) and 11 out of 34 patients in stage III (32.4%) were from age group 66-75 years.

TABLE 39 STAGE TO SERUM ALBUMIN

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
Serum Albumin (gm/dl)	**<3.5**	5	17.9 %	30	88.2 %	35	0.070	0.000
	>3.5	23	82.1 %	4	11.8 %	27		
	Total	28	100.0 %	34	100.0	62		

In our study, 5 patients out of 28 patients of stage II had serum albumin <3.5gm/dL (17.9%) and 30 patients out of 34 patients of stage III (88.2%) had serum albumin <3.5gm/dL. 23 out of 28 patients of stage II (82.1%) had serum albumin >3.5gm/dL and 4 out of 34 patients in stage III had serum albumin >3.5 gm/dL. (11.8%) (p value-0.00)

TABLE 40 STAGE TO SERUM TOTAL PROTEIN

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
Serum Total Protein (gm/dl)	4 to 6	3	10.7%	7	20.6%	10	1.91	0.387
	6 to 9	20	71.4%	24	70.6%	44		
	>9	5	17.9%	3	8.8%	8		
	Total	28	100.0 %	34	100.0 %	62		

In our study , 20 out of 28 patients (71.4%) is stage II had total serum protein within 6-9 gm/dL and 24 out of 34 patients had total serum protein of 6-9 gm/dL (70.6%), 5 patients in stage II (17.9%) and 3 patients in stage III (8.8%) had serum protein >9gm/dL (8.8%). 3 patients (10.7%) in stage II and 7 patients out of 34 patients in stage III had total serum protein of 4-6gm/dL (20.6%). P value of this correlation is 0.387 (not significant).

TABLE 41 STAGE TO SERUM GLOBULIN

		Stage				Total	Chi-square value	p-value
		Stage II	Stage II	Stage III	Stage III			
GLOBULIN (gm/dl)	< 2	2	7.10%	0	0.00%	2	3.317	0.19
	2-3.5	8	28.60%	7	20.60%	15		
	> 3.5	18	64.30%	27	79.40%	45		
	Total	28	100.0%	34	100.0	62		

In our study, 2 out of 28 patients in stage II (7.10%) had serum globulin <2gm/dL whereas no patient in stage III had this range of serum globulin value. It was found that 8 out of 28 patients of stage II (28.60%) had serum globulin 2-3.5 gm/dL and 7 out of 34 patients in stage III (20.60%) had serum globulin between 2-3.5 g/dL.18 out of 28 patients in stage II (64.30%) had serum globulin more than 3.5 gm/dL and 27 out of 34 patients in stage III (79.40%) had serum globulin more than 3.5 gm/dL.

TABLE 42 STAGE TO A/G RATIO

		Stage				Total	Chi-square value	p-value
A/G RATIO		Stage II	Stage II	Stage III	Stage III		4.433	0.109
	< 1.1	20	71.40%	31	91.20%	51		
	1.1-2.5	7	25.00%	3	8.80%	10		
	> 2.5	1	3.60%	0	0.00%	1		
		28	100%	34	100%	62		

In our study, 20 patients out of 28 patients in stage II (71.4%) had A/G ratio <1.1 and, 31 out of 34 patients in stage III had A/G ratio <1.1 (91.2%). 7 patients out of 28 patients in stage II (25.0%) and 3 patients out of 34 patients in stage III had A/G ratio 1.1-2.5 (8.8%).1 patient out of 28 patients in stage II had serum albumin to globulin ratio> 2.5 (3.6%) but no patient in stage III had this range of A/G ratio. Thus, A/G ratio reversal had no significant correlation with stage III and prognosis (p value- 0.109) in our study.

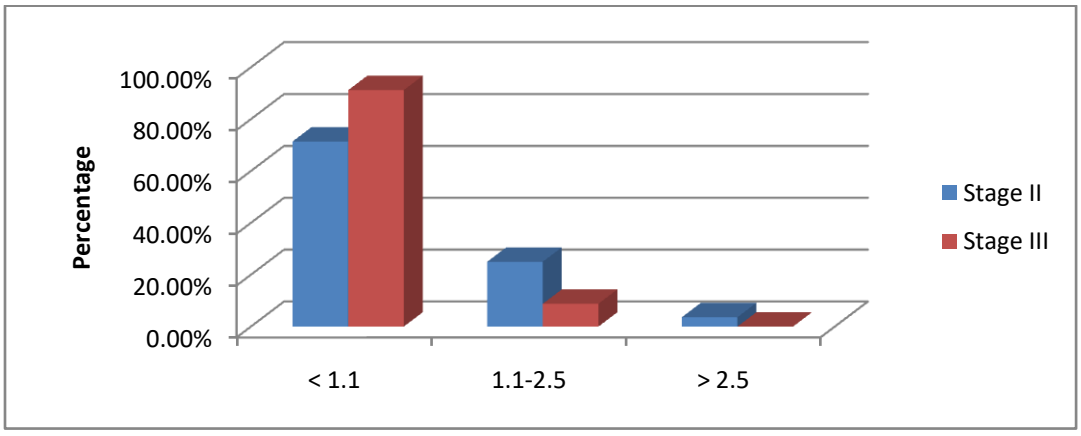

FIGURE 31 STAGE TO A/G RATIO CORRELATION

TABLE 43- STAGE TO MOLECULAR PROFILE

		Stage				Total	Chi-square value
		Stage II	Stage II	Stage III	Stage III		
Molecular Profile	Negative	12	42.90%	17	50.00%	29	0.842
	Molecular Profile t [4:14]	5	17.90%	5	14.70%	10	
	Molecular Profile t [11:14]	6	21.40%	7	20.60%	13	
	Molecular Profile t [14:16]	4	14.30%	3	8.80%	7	
	Molecular Profile p53 del [17p13 del]	1	3.60%	2	5.90%	3	
Total		28	100.00%	34	100.00%	62	

In our study. it was observed that 5 out of 34 patients (14.7%) in stage III and 5 out of 28 patients (17.9%) in stage II had Molecular Profile- t [4:14] positive, 7 patients in stage III (20.6%) and 6 patients in stage II (21.4%) had t(11:14) positive, 3 out of 34 patients (8.8%) in stage III and 4 out of 28 patients (14.3%) in stage II had t(14:16) positive, 2 patients (5.9%) in stage III and 1 patient (3.6%) in STAGE II had p53 del positive.

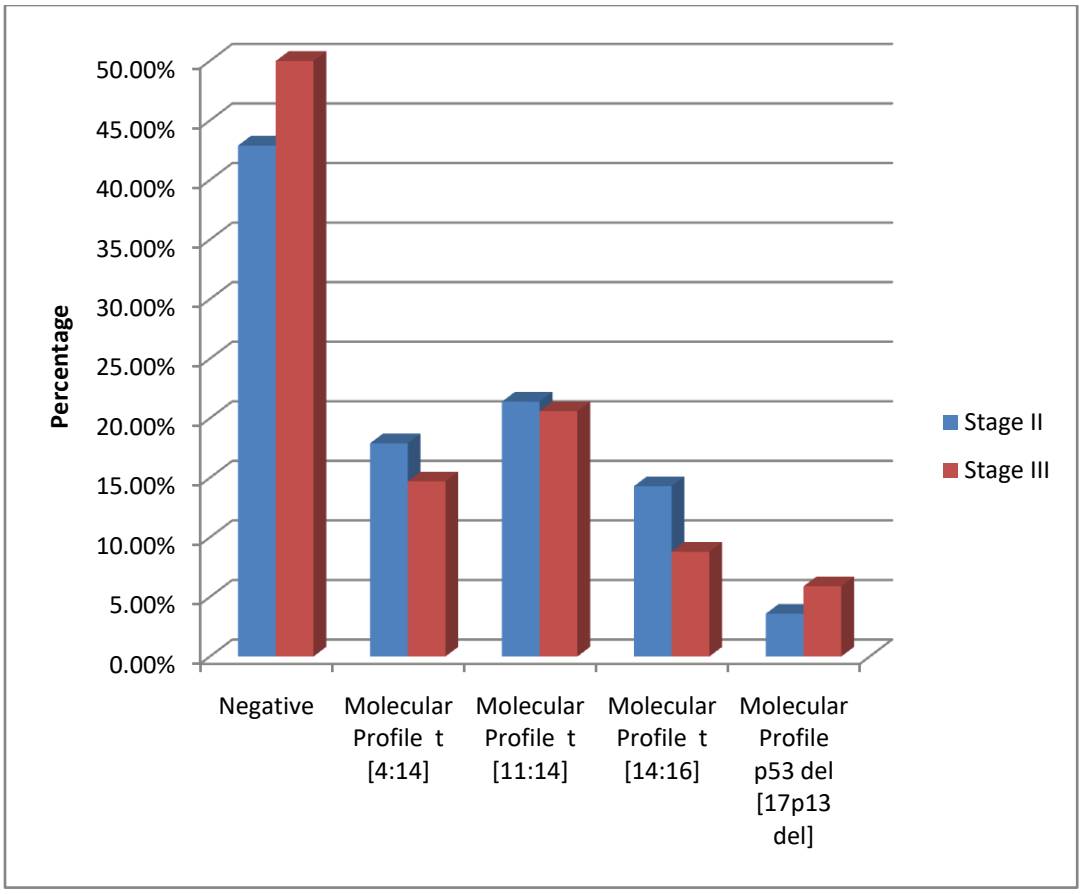

FIGURE 32- STAGE TO MOLECULAR PROFILE CORRELATION

TABLE 44 STAGE TO BETA 2 MICRO GLOBULIN (mg/l)

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
Beta 2 microglobulin	<3.5	13	46.4%	0	0.00%	13	0.019	0.000
	>3.5	15	53.6%	34	100%	49		
	Total	28	100.0%	34	100%	62		

In our study, 13 out of 28 patients (46.4%) in stage II had beta-2-microglobulin <3.5 mg/l but no patient in stage III had this range of value of beta-2-microglobulin. It was found that 15 out of 28 patients in stage II (53.6%) had serum beta-2-microglobulin >3.5mg/l and all patients (100%) of patients in stage III had serum beta-2-microglobulin>3.5mg/l. So, beta 2 microglobulin had positive correlation with staging and prognosis (p value-0.00)

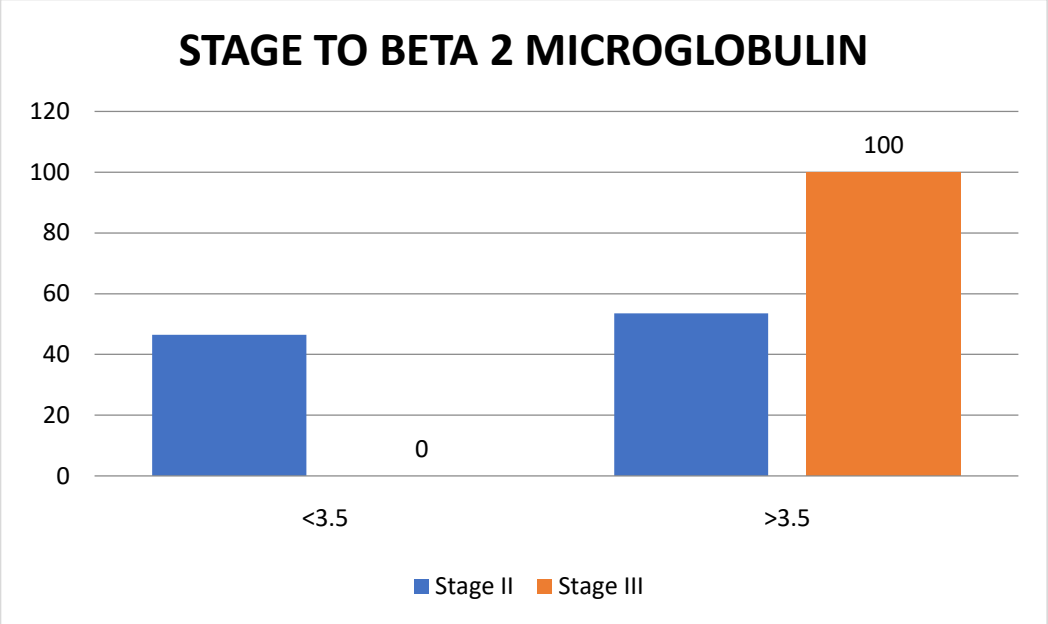

FIGURE 33- STAGE TO BETA 2 MICROGLOBULIN

TABLE 45 STAGE TO SERUM LDH

		Stage				**Total**	**Chi-square value**	**p-value**
		Stage II		**Stage III**				
Serum LDH (U/L)	**<225**	20	71.4%	0	0.00 %	20	0.139	0.000
	>225	8	28.6%	34	100.0 %	42		
	Total	28	100.0%	34	100.0	62		

In our study, it was observed that all patients of stage III serum LDH levels >225 U/L (100%) whereas in stage II, 8 out of 28 patients (28.6%) had serum LDH>225 U/L whereas 20 patients out of 28 patients in stage II (71.4%) had serum LDH <225 U/L (71.4%) and no patient in stage III (0%) had this range of serum LDH value. Thus, high levels of serum LDH >225 U/L is strongly associated with staging and poor prognosis (p value 0.000).

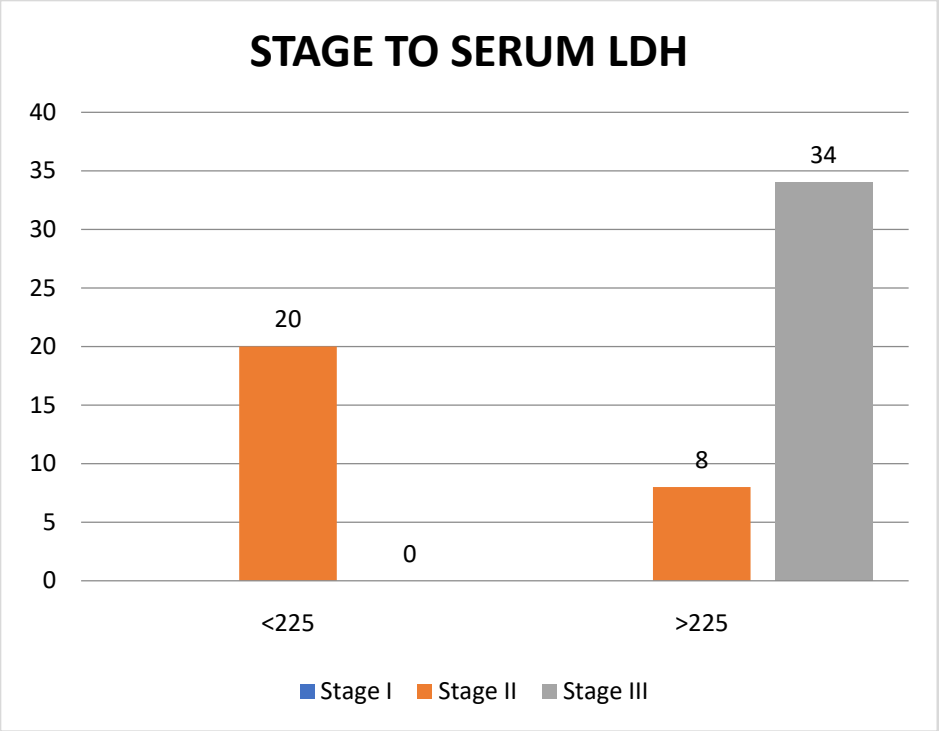

FIGURE 34- STAGE TO SERUM LDH CORRELATION

TABLE 46 STAGE TO HB

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
HB (gm /dl)	<8	0	0.0%	24	70.6%	24	32.267	0.001
	8 to 10	16	57.1%	6	17.6%	22		
	>10	12	42.9%	4	11.8%	16		
	Total	28	100.0	34	100.0%	60		

In our study it was found that no patient in stage II had Hb <8g/dl but 24 out of 34 patients in stage III had Hb<8g/dL(70.6%), 16 patients out of 28 in stage II (57.1%) had Hb 8-10 g/dl but only 6 out of 34 patients in stage III had value of Hb in this range (17.6%). 12 out of 28 patients in stage II had value of Hb>10g/dL (42.9%) but 4 patients out of 34 patients in stage III(11.8%) had value of Hb >10 g /dl (11.8%)

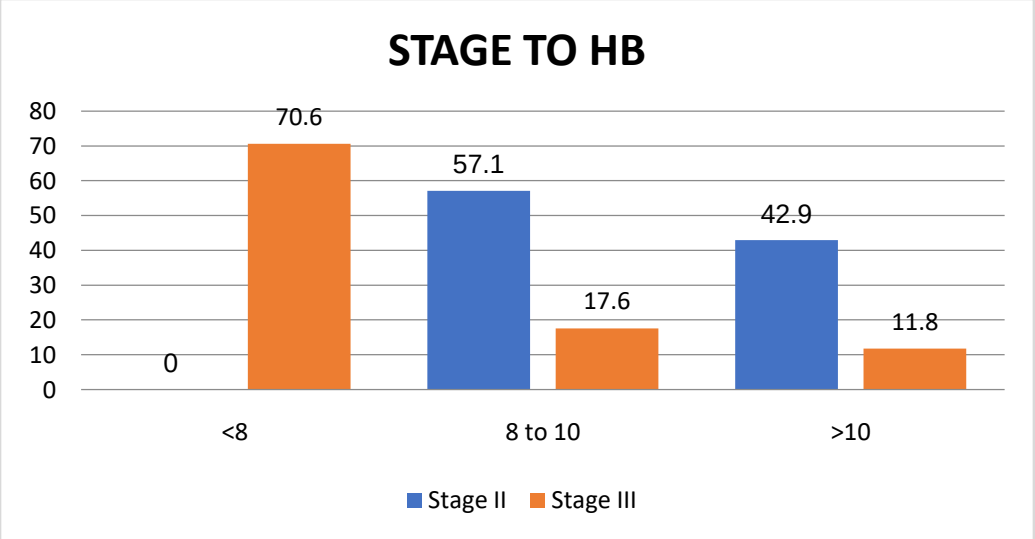

FIGURE 35- STAGE TO HB CORRELATION

TABLE 47 STAGE TO TLC

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
TLC	< 4	3	10.7%	4	11.8%	7	0.493	0.61
	4 to 11	20	71.4%	24	70.6%	44		
	> 11	5	17.9%	6	17.6%	11		
	Total	28	100.0%	34	100.0%	62		

In our study , it was found that 3 out of 28 patients in stage II of Multiple myeloma (10.7%) and 4 out of 34 patients in stage III (11.8%) to have leucopenia (TLC<4 x $10^3/mm^3$). 20 out of 28 patients in stage II (71.4%) and 24 out of 34 patients in stage III to have TLC within 4-11 x $10^3/mm^3$ (70.6%). 5 patients out of 28 patients in stage II had leucocytosis with TLC x $10^3/mm^3$ (17.9%) whereas 6 patients out of 34 patients in stage III had leucocytosis (TLC> 11 x $10^3/mm^3$). P value of this relationship is 0.61 (not statistically significant)

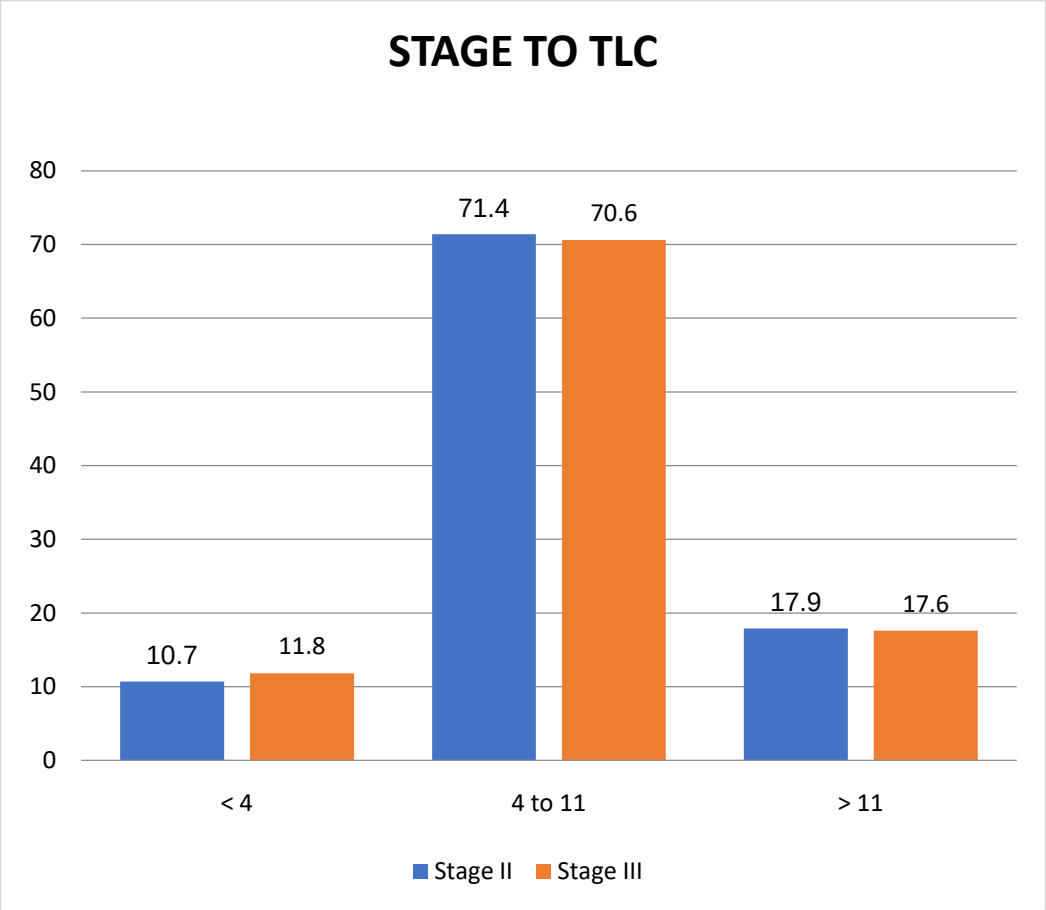

FIGURE 36- STAGE TO TLC CORRELATION

TABLE 48 STAGE TO PLATELET COUNT

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
Platelet Count	**<1.5 Lakh/** mm^3	5	17.9%	11	32.4%	16	0.470	0.051
	>1.5 Lakh/ mm^3	23	82.1%	23	67.6%	46		
	Total	28	100.0%	34	100.0%	62		

23 out of 28 patients of stage II of multiple myeloma (82.1%) had no thrombocytopenia (platelet count > 1.5 lakh/ mm^3) and 23 out of 34 patients (67.6%) in stage III had no thrombocytopenia. Only 5 patients out of 28 patients in stage II (17.9%) had thrombocytopenia (platelet count < 1.5 lakh/ mm^3), whereas 11 out of 34 patients in stage III (32.4%) had thrombocytopenia. This correlation has not been found to be significant as per our study (p value-0.051)

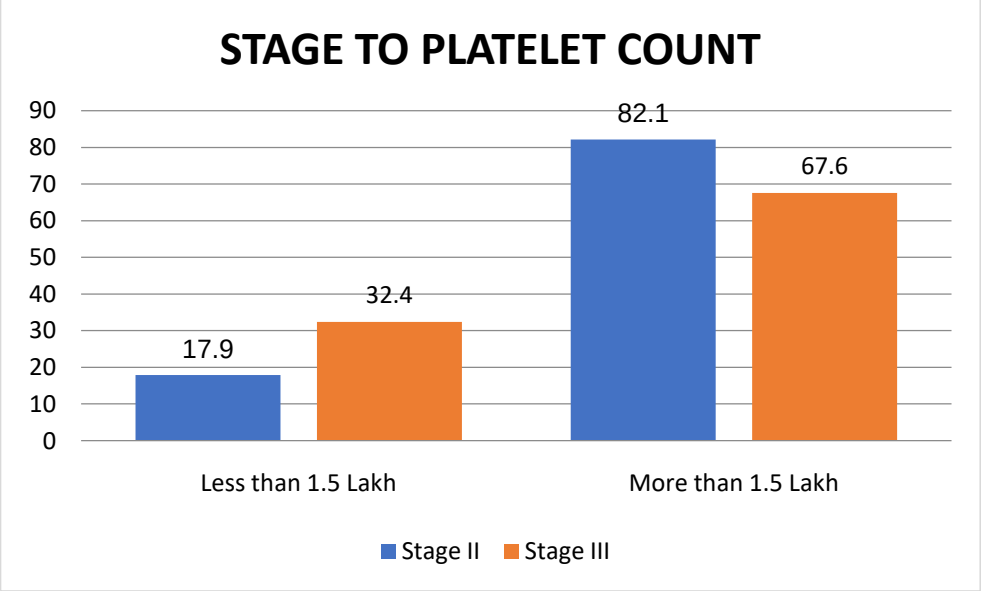

FIGURE 37 STAGE TO PLATELET COUNT CORRELATION

TABLE 49 STAGE TO PBF

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
PBF	**RF+**	16	57.1%	22	64.7%	38	1.477	0.688
	RF-	12	42.9%	12	35.3%	24		
	Total	28	100.0%	34	100.0%	62		

In our study, it was found that maximum patients who were in stage II of multiple myeloma had Rouleaux formation (16 out of total 28 patients of stage II)[57.1%] In stage III, 22 (majority) out of total, 34 patients (64.7%) had Rouleaux formation . 12 patients out of 34 patients of stage III [42.9%] had no rouleaux formation. No patient in stage II had thrombocytopenia in our study. However, Rouleaux formation and staging of Multiple myeloma had no significant correlation as per our study. (p value – 0.688)

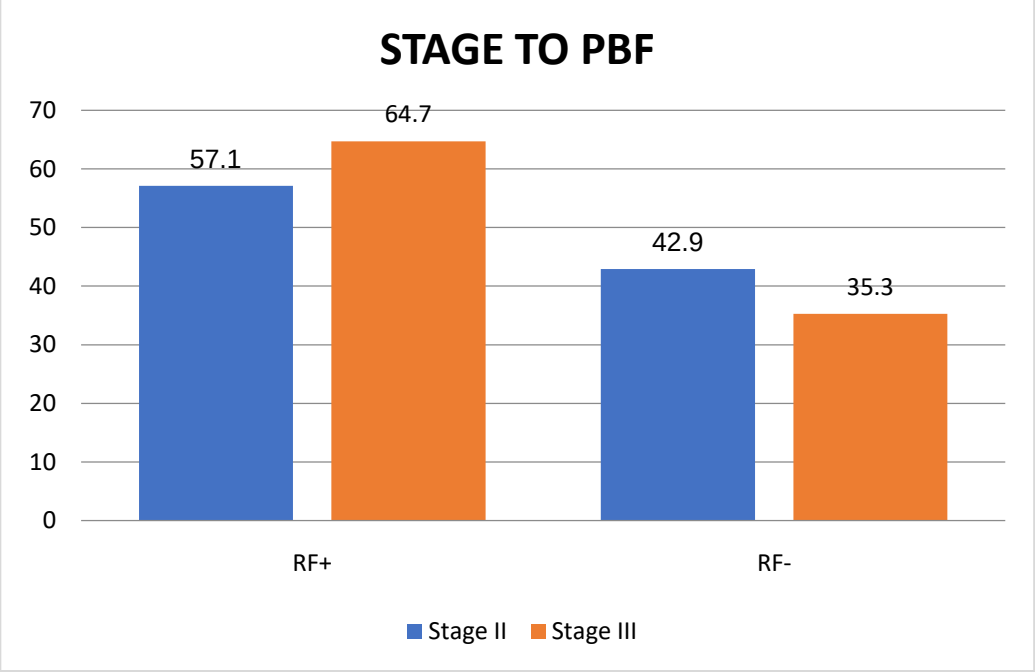

FIGURE 38- STAGE TO PBF CORRELATION

STAGE 50 STAGE TO ESR

		Stage				**Total**	**Chi-square value**	**p-value**
		Stage II		**Stage III**				
ESR	20 to 50	3	10.72%	4	11.75%	7	0.0345	0.049
	50 to 100	5	17.85%	6	17.65%	11		
	>100	20	71.43%	24	70.60%	44		
	Total	28	100.0%	34	100.0%	62		

In our study, it was found that ESR was within 20-50mm/hour in 3 out of 28 patients of stage II (10.72%) and 4 out of 34 patients in stage III (11.75%). ESR was found to be within 50-100 mm per hour in 5 out of 28 patients in stage II (17.85%) and 6 out of 34 patients in stage III (17.65%). ESR was found to be more than 100 mm / hour in 20 out of 34 patients in stage II (71.43%) and 24 out of 34 patients in stage III (70.60%). So, there was no correlation between ESR and staging according to our study (p value 0.049)

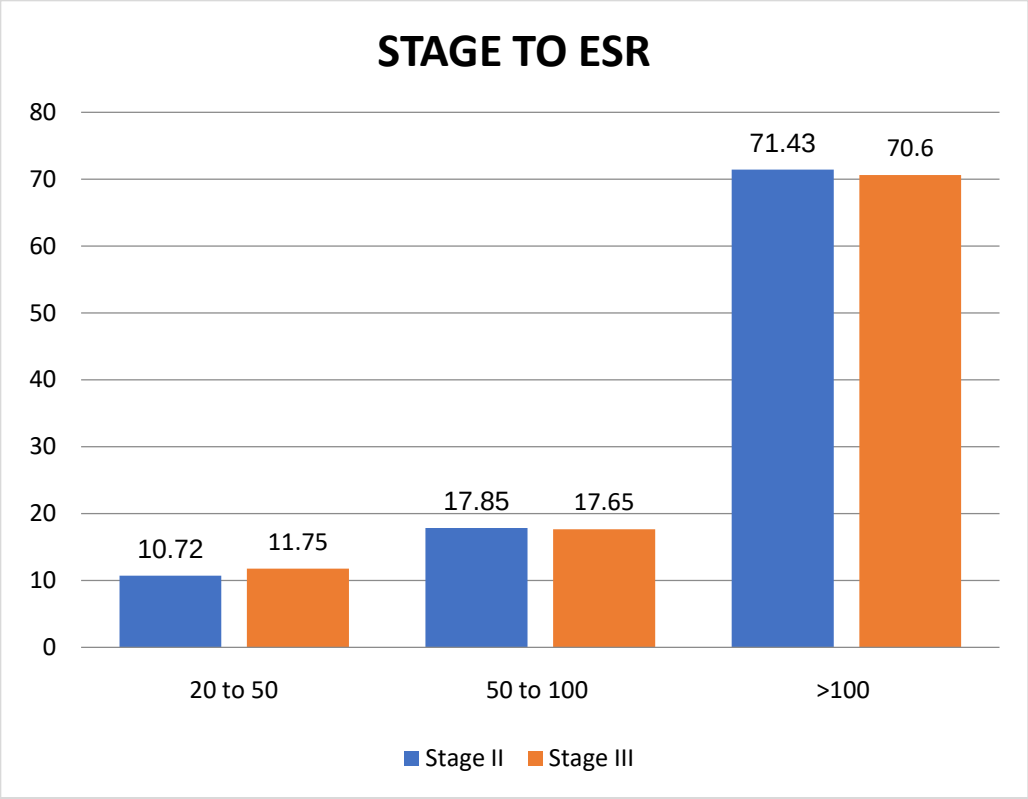

FIGURE 39- STAGE TO ESR CORRELATION

TABLE 51 STAGE TO ALKALINE PHOSPHATASE

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
Alkaline Phosphatase	<129	23	82.1%	31	91.2%	54	1.115	0.291
	>129	5	17.9%	3	8.8%	8		
	Total	28	100.0%	34	100.0%	62		

In our study, 23 out of 28 patients in stage II of multiple myeloma had normal ALP (40-129U) [82.1%] whereas 31 out of 34 patients in stage III [91.2%] had normal ALP (40-129U). Only 5 out of 24 patients of stage II had elevated ALP of > 129 [17.9%] and 3 out of 34 patients [8.8%] in stage III had elevated ALP (>129U). This correlation is insignificant (p value 0.291)

TABLE 52 STAGE TO CORRECTED CALCIUM

		Stage				Total	Chi-square value	p-value
		Stage II	Stage II	Stage III	Stage III			
CORRECTED CALCIUM	8.5-10.3	1	3.6%	0	0.0%	1	1.357	0.507
	10.3-11	4	14.3%	4	11.8%	8		
	> 11	23	82.1%	30	88.2%	53		

It was found in our study that in stage II, 23 out of 28 patients (82.1%) had hypercalcemia i.e serum calcium >11mg/dl and in stage III, 30 out of 34 patients (88.2%) had serum calcium >11mg/dl, 4 out of 28 patients(14.3%) in stage II had serum calcium 10.3-11mg/dl and 4 out of 34 patients (11.8%) had serum calcium 10.3-11mg/dl in stage II , 1 out of 28 patients had serum calcium 8.5-10.3 mg/dl (3.6%) in stage II and no patient in stage III had serum calcium 8.5-10.3 mg/dl.

FIGURE 40 STAGE TO SERUM CALCIUM CORRELATION

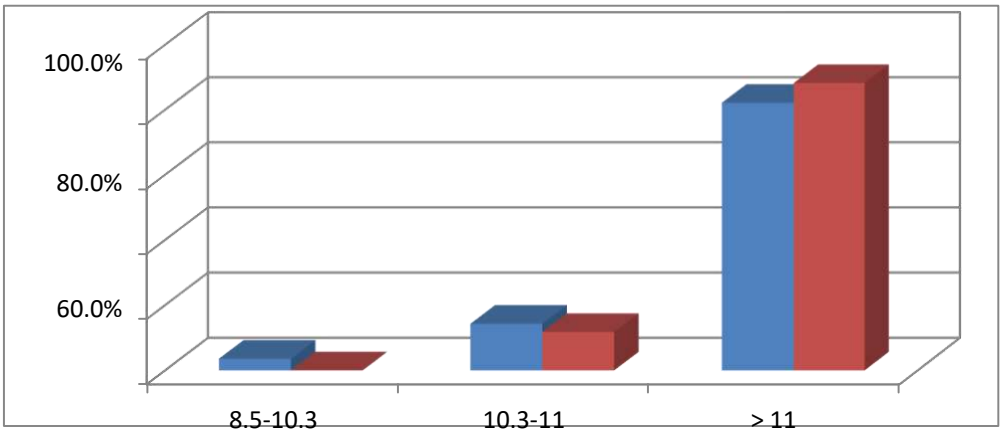

TABLE 53 STAGE TO SERUM CREATININE

		Stage				Total	Chi-square value	p-value
		StageII		StageIII				
SerumCreatinine	<2	11	39.3	10	29.4	54	0.668	0.414
	>2	17	60.7	24	70.6	8		
	Total	28	100.0%	34	100.0%	62		

It was observed that 17 out of 28 patients (60.7%) in stage II and 24 out of 34 patients (70.6%) in stage III had serum creatinine > 2mg/dl and 11 out of 28 patients (39.3%) in stage II and 10 out of 34 patients (29.4%) in stage III had serum creatinine <2mg /dl.. (p value– 0.414)

FIGURE 41 STAGE TO SERUM CREATININE CORRELATION

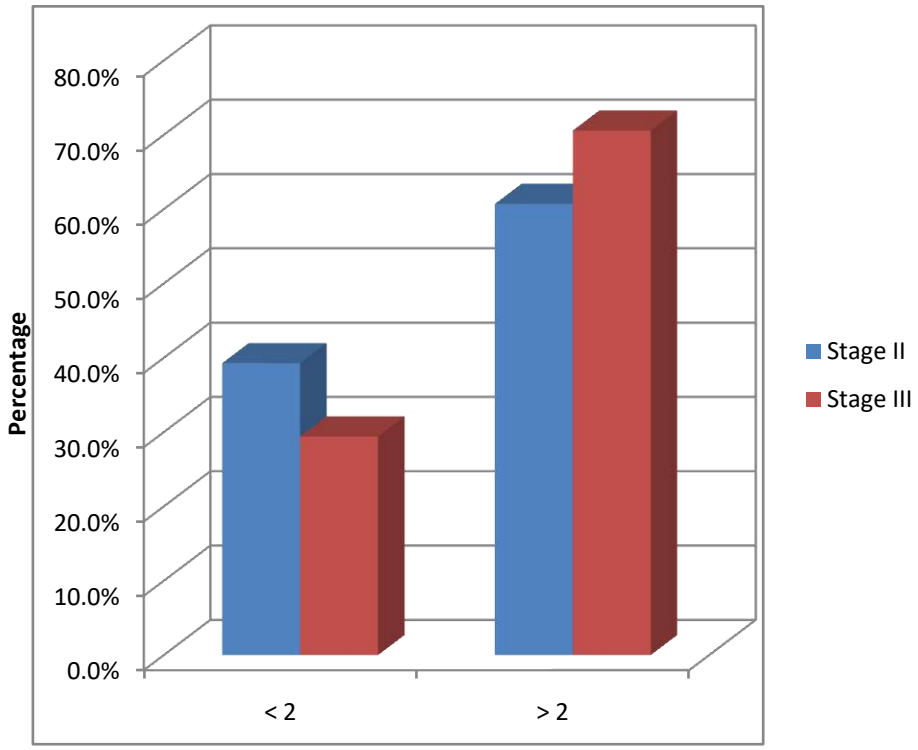

TABLE 54 STAGE TO SKELETAL SURVEY / PET-CT

		Stage				Total	Chi-square value	p-value
		Stage II		Stage III				
Skeletal Survey/PET-CT Scan	**Fracture**	5	17.9	3	8.8	8	1.115	0.291
	Non Fracture	23	82.1	31	91.2	54		
	Total	28	100.0%	34	100.0%	62		

In our study, 5 out of 28 patients (17.9%) in stage II had fractures on skeletal survey and 3 out of 34 patients in stage III (8.8%) had fractures.So there was no significant correlation between fractures and staging (p value- 0.291).

FIGURE 42 STAGE TO SKELETAL SURVEY / PET-CT Correlation

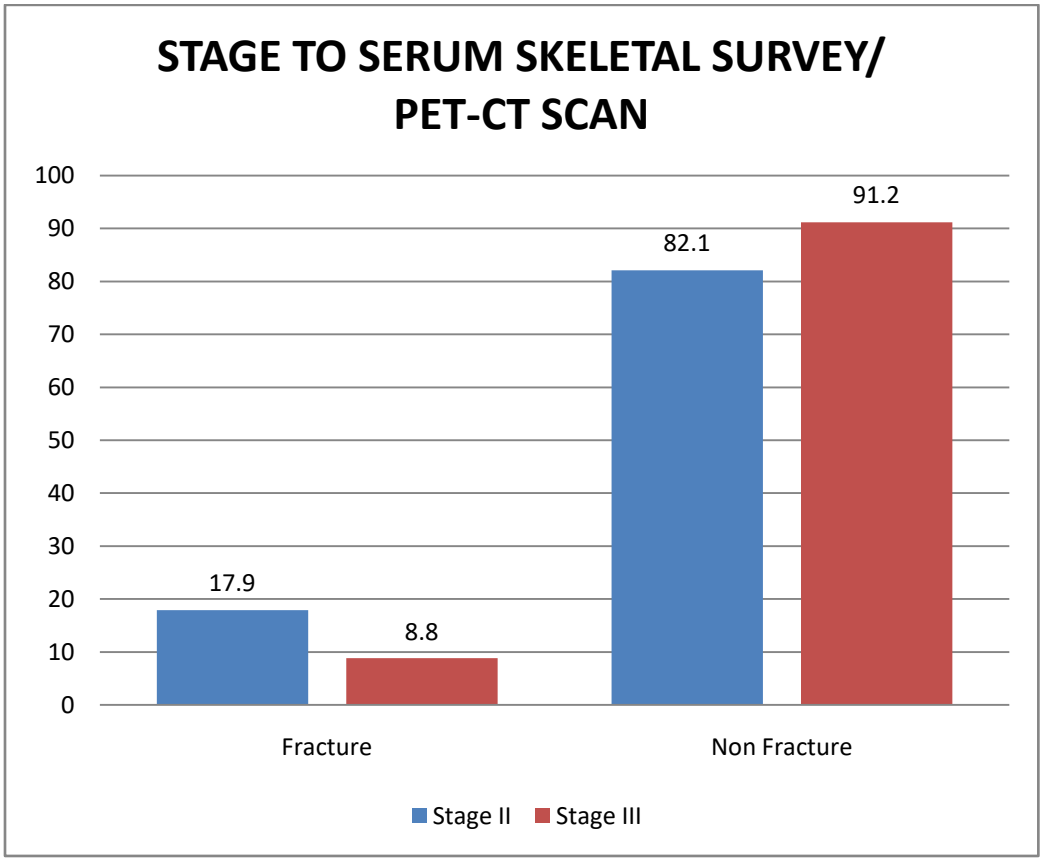

TABLE 55 SKELETAL SURVEY/ PET-CT SCAN TO ALKALINE PHOSPHATASE

		Skeletal Survey/ PET-CT Scan				Total		Chi-square value	p-value
		Fracture		Non Fracture					
Alkaline Phosphatase	<129	1	12.5%	54	100.%	55	100.0%	53.264	0.001
	>129	7	87.5%	0	0.00%	7	100.0%		
	Total	28	100.0%	34	100.0%	62			

In our study it was found that out of 62 patients, 8 patients had elevated ALP (>129U/L) , out of which 7 patients had fracture on skeletal survey [87.5%] and 1 had no evidence of fracture on skeletal survey[12.5%]. So, raised alp levels [>129U/L] had significant correlation with fractures on skeletal survey [p value -0.001].

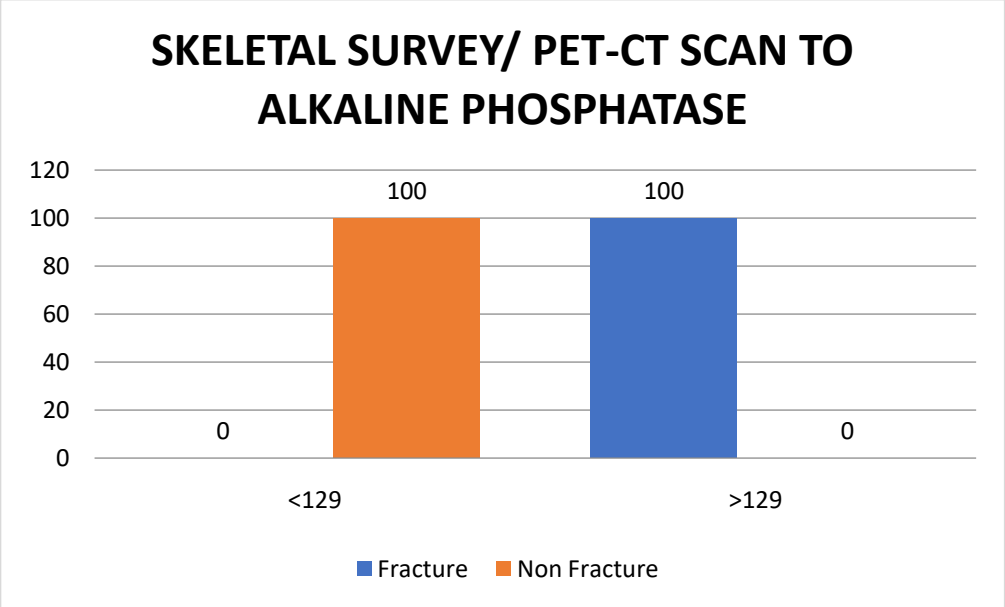

FIGURE 43 SKELETAL SURVEY/ PET-CT SCAN TO ALKALINE PHOSPHATASE CORRELATION

TABLE 56 STAGE TO BONE MARROW STUDY

		Stage				Total	Chi-square value	p-value
		Stage II	Stage II	Stage III	Stage III			
Bone Marrow Aspirate/ Biopsy	NORMAL	1	3.60%	2	5.90%	3	1.386	0.5
	PLASMA CELL DYSCRASIA	26	92.90%	32	94.10%	58		
	PLASMA CELL PROMINENCE	1	3.60%	0	0.00%	1		
Total		28	100.00%	34	100.00%	62		

In stage II , 26 out of 28 patients had plasma cell dyscrasia (92.9%) whereas in stage III, 32 out of 34 patients had plasma cell dyscrasia (94.1%), 1 patient out of 28 patients in stage II had plasma cell prominence (3.6%) but no patient in stage III had this feature. 1 patient in stage II had normal marrow (3.6%) and 2 had normal marrow(5.9%) in stage III. So, bone marrow study has no significant correlation with staging or prognosis (p value- 0.5).

The parameters like age, sex, serum creatinine, serum albumin etc. were compared between patients who died vs the ones who got discharged/ DAMA.

TABLE 57 OUTCOME TO AGE

		Outcome		
AGE		**Death**	**Discharge/DAMA**	**Total**
	35 to 45 year	0 (0.00)	4 (6.8%)	4
	46 to 55 year	0 (0.00)	7 (11.9%)	7
	56 to 65 year	3 (100.0%)	28 (47.5%)	31
	66 to 75 year	0(0.00)	20 (33.9%)	20
	Total	3 (100.0%)	59 (100.0%)	62

In our study, all the 3 patients (100.0%) who died were in the age group of 56 to 65 years and 28 (47.5%) out of 59 patients who were discharged/ DAMA were in the age group 56 to 65 year followed by 20 patients (33.9%) in the age group 66 to 75 year followed by 7 patients (11.9%) in the age group of 46 to 55 year and 4 patients (6.8%) in the age group of 35 to 45 year.

TABLE 58 OUTCOME TO HB

		Outcome		
HB (gm/dl)		**Death**	**Discharge/ DAMA**	**Total**
	<8	1 (33.3%)	22 (37.3%)	23
	8 to 10	1 (33.3%)	28 (47.5%)	29
	>10	1 (33.3%)	9 (15.3%)	10
	Total	**3 (100.0%)**	**59 (100.0%)**	**6**

In our study, HB <8gm/dl was found in 1 (33.3%) out of 3 patients who died and 22 (37.3%) out of 59 patients who were discharged/ DAMA. HB between 8 to 10gm/dl was found in 1 (33.3%) out of 3 patients who died and 28 (47.5%) out of 59 patients who were discharged/ DAMA. HB >10 gm/dl was found in 1 (33.3%) out of 3 patients who died and 9 (15.3%) out of 59 patients who were discharged/ DAMA.

TABLE 59 OUTCOME TO ESR

		Outcome		
ESR (mm/hr)		**Death**	**Discharge/ DAMA**	**Total**
	20 to 50	1 (33.3%)	6 (10.2%)	7
	50 to 100	2 (66.7%)	42 (71.2%)	44
	>100	0	11 (18.6%)	11
	Total	**3 (100.0%)**	**59 (100.0%)**	**62**

In our study, ESR between 20 to 50 mm/hour was found in 1 (33.3%) out of 3 patients who died and 6 (10.2%) out of 59 patients who got discharged/ DAMA. ESR between 50 to 100 mm/hour was found in 2 (66.7%) out of 3 patients who died and 42 (71.2%) out of 59 patients who got discharged/ DAMA. ESR >100 mm/hourwas not found in any patient who died and was found in 11 (18.6%) out of 59 patients who got discharged/ DAMA.

TABLE 60 OUTCOME TO PLATELET COUNT

	Outcome			
PLATELET COUNT		**Death**	**Discharge/ DAMA**	**Total**
	< 1.5 Lakh/ mm^3	1 (33.3%)	15 (25.4%)	16
	> 1.5 Lakh/ mm^3	2 (66.7%)	44 (74.6)%	46
	Total	3 (100.0%)	59 (100.0%)	62

In our study, Platelet count <1.5 lakh/mm^3 was found in 1 (33.3%) out of 3 patients who died and 15 (25.4%) out of 59 patients who got discharged/ DAMA. Platelet count >1.5 lakh/mm^3 was found in 2 (66.7%) out of 3 patients who died and 44 (74.6%) out of 59 patients who got discharged/ DAMA.

TABLE 61 OUTCOME TO TLC

	Outcome			
TLC		**Death**	**Discharge/ DAMA**	**Total**
	< 4	0 (0.0%)	7 (11.9%)	7
	4 to 11	3 (100.0%)	41 (69.5%)	44
	> 11	0 (0.0%)	11 (18.9%)	11
	Total	3 (100.0%)	59 (100.0%)	62

In our study, 3 patients (100.0%) who died had TLC between 4 to 11x $10^3/mm^3$ and out of 59 patients who got discharged/ DAMA, 41 patients (69.5%) had TLC between 4 to 11x $10^3/mm^3$ followed by 11 patients (18.9%) who had TLC > 11x$10^3/mm^3$ and 7 patients (11.9%) had TLC < 4 x $10^3/mm^3$,

TABLE 62 OUTCOME TO CREATININE

	Outcome			
S.Creatinine (mg/dl)		**Death**	**Discharge/ DAMA**	**Total**
	<2	1 (33.3%)	20 (33.9%)	21
	>2	2 (66.7)	39 (66.1%)	41
	Total	3 (100.0%)	59 (100.0%)	62

In our study, Serum creatinine <2mg/dl was found in 1 (33.3%) out of 3 patients who died and 20 (33.9%) out of 59 patients who got discharged/ DAMA. Serum creatinine >2mg/dl was found in 2(66.7%) out of 3 patients who died and 39 (66.1%) out of 59 patients who got discharged/ DAMA.

TABLE 63 OUTCOME TO CALCIUM

	Outcome			
CORRECTED CALCIUM (mg/dl)		**Death**	**Discharge/ DAMA**	Total
	8.5-10.2	0 (0.00%)	1 (1.7%)	1
	10.3-11	1 (33.3%)	7 (11.9%)	8
	> 11	2 (66.7%)	51 (86.4%)	53
	Total	3 (100.0%)	59 (100.0%)	62

In our study, serum calcium of >11mg/dl was found in 2 (66.6%) out of 3 patients who died and 51 (86.4%) out of 59 patients who got discharged/ DAMA. Serum calcium of 10.3-11mg/dl was found in 1 (33.3%) out of 3 patients who died and 8 (11.9%) out of 59 patients who got discharged/ DAMA. Serum calcium of 8.5-10.2mg/dl was found in only 1(1.7%) out of 59 patients who got discharged/ DAMA.

TABLE 64 OUTCOME TO SERUM ALBUMIN

	Outcome			
Serum Albumin (gm/dl)		**Death**	**Discharge/ DAMA**	Total
	<3.5	2 (66.7%)	33 (55.9%)	35
	>3.5	1 (33.3%)	26 (44.1%)	27
	Total	3 (100.0%)	59 (100.0%)	62

Hypoalbuminemia {serum albumin<3.5gm/dl) was seen in 2 out of 3 patients (66.7%) who died vs 33 out of 59 patients (55.9%) who got discharged/ DAMA. Serum albumin >3.5gm/dl was seen in 1 out of 3 patients (33.3%) who died vs 26 out of 59 patients (44.1%) who got discharged/ DAMA .

TABLE 65 OUTCOME TO A/G RATIO

		Outcome				Total
		Died		DISCHARGE/ DAMA		
A/G RATIO	< 1.1	3	100.0%	48	81.4%	51
	1.1-2.5	0	0.0%	10	16.9%	10
	> 2.5	0	0.0%	1	1.7%	1

In our study, A/G ratio reversal was seen in all the 3 patients (100%) who died vs. 48 out of 59 patients (81.4%) who got discharged/ DAMA. A/G ratio of 1.1-2.5 was seen in 10 out of 59 patients (16.9%) who got discharged/ DAMA and 1 out of 59 patients (1.7%) who got discharged/ DAMA had A/G ratio of >2.5.

TABLE 66 OUTCOME TO Serum LDH (IU/L)

	Outcome			
Serum LDH(IU/L)		**Death**	**Discharge/ DAMA**	Total
	<225	0	20 (33.9%)	20
	>225	3 (100.0%)	39 (66.1%)	42
	Total	3 (100.0%)	59 (100.0%)	62

High LDH (>225 IU/L) was seen in all the 3 patients who died (100%) vs 39 out of 59 patients (66.1%) who got discharged/ DAMA. LDH <225IU/L was seen in 20 out of 59 patients (33.9%) whogot discharged/ DAMA.

TABLE 67 OUTCOME TO BETA 2 MICROGLOBULIN

	Outcome			
		Death	**Discharge/ DAMA**	Total
BETA 2 MICROGLOBULIN (mg/l)	< 3.5	0	13 (22.0%)	13
	3.5-5.5	1 (33.3%)	14 (23.7%)	15
	> 5.5	2 (66.7%)	32 (54.2%)	34
	Total	3 (100.0%)	59 (100.0%)	62

Beta 2 micro globulin was >5.5 mg/l in 2 out of 3 patients (66.7%) who died vs. 32 out of 59 patients (54.2%) who got discharged/ DAMA. Beta 2 micro globulin was 3.5-5.5 mg/l in 1 out of 3 patients (66.7%) who died vs 14 out of 59 patients (23.7%) who got discharged/ DAMA. Beta 2 micro globulin was <3.5 mg/l in 13 out of 59 patients (22.0%) who got discharged/ DAMA.

TABLE 68 Outcome to Bone Marrow Aspirate / Biopsy

		Outcome		Total
		Death	**Discharge/ DAMA**	
Bone Marrow Aspirate / Biopsy	Normal	0 (0.00)%	3 (5.09%)	3
	Plasma Cell Dyscrasia	3 (100.0%)	55 (93.22%)	58
	Plasma Cell Prominence	0 (0.00)%	1 (1.69%)	1
	Total	3 (100.0%)	59	62

In our study, plasma cell dyscrasia was found in all 3 patients who died (100%) and 55 out of 59 patients (93.2%) who got discharged/ DAMA on bone marrow examination.. Out of 59 patients who got discharged/ DAMA, 1 patient had plasma cell prominence (1.7%) and 3 patients had normal bonemarrow (5.1%).

The parameters like age, sex, serum creatinine, serum albumin etc. were compared between the patients with molecular profile positive or negative.

TABLE 69A. Molecular Profile vs. Various Parameters

		MOLECULAR PROFILE				Total	Chi-square value/Z	p-value
		NO		YES				
MEAN AGE		61.40	6.841	61.84	9.916		**-0.204**	**0.839**
Sex	F	11	36.7%	15	46.9%	26	0.663	0.416
	M	19	63.3%	17	53.1%	36		
HB	< 10	24	80.0%	22	68.8%	46	1.118	0.572
Platelet count	<1.5 Lakh	7	23.3%	9	28.1%	16	0.186	0.667
ESR	< 50	4	13.3%	3	9.4%	7	0.26	0.878
	50 to 100	21	70.0%	23	71.9%	44		
	> 100	5	16.7%	6	18.8%	11		
TLC	< 4	4	13.3%	3	9.4%	7	0.533	0.766
	4-11.0	20	66.7%	24	75.0%	44		
	> 11	6	20.0%	5	15.6%	11		

The molecular profile was compared with various demographic and biochemical parameters. 33 out of 62 had molecular profile positive whereas it was negative in 29 out of 62 patients. The mean age was 61.4 years in group with negative molecular profile and 61.84 years in group with positive molecular profile. In both the groups, males were more than females. Anemia (Hb<10gm/dl) was seen in 80% of patients in group with negative molecular profile and 68.8% in group with positive molecular

profile. Thrombocytopenia (<1.5lakh/mm^3) was seen in 23.3% of patients in group with negative molecular profile and 28.1% in group with positive molecular profile. Raised ESR (>50) was seen in 86.7% patient in group with negative molecular profile and 90.7% patients in group with positive molecular profile. Leucopenia was seen in 13.3% of patients in group with negative molecular profile and 9.4% in group with positive molecular profile. Leucocytosis was seen in 20.0% patients in group with negative molecular profile and 15.6% patients in group with positive molecular profile.

TABLE 69B. Molecular Profile vs. Various Parameters

Serum Creatinine	<2	11	36.7%	10	31.3%	21	0.203	0.652
	>2	19	63.3%	22	68.8%	41		
CORRECTED CALCIUM	> 11	26	86.7%	27	84.4%	53	0.955	0.620
Serum Albumin	<3.5	20	66.7%	20	62.5%	40	0.117	0.732
	>3.5	10	33.3%	12	37.5%	22		
A/G RATIO	< 1.1	25	83.3%	26	81.3%	51	0.956	0.620
	1.1-2.5	5	16.7%	5	15.6%	10		
	> 2.5	0	0.0%	1	3.1%	1		

Renal Failure i.e. Serum creatinine >2mg/dl was seen in 63.3% of patients in group with negative molecular profile and 68.8% in group with positive molecular profile. Corrected calcium >11mg/dl was seen in 86.7% patients in group with negative molecular profile and 84.4% in group with positive molecular profile. Hypoalbuminemia (serum albumin<3.5gm/dl) was seen in 66.7% patients in group with negative molecular profile and 62.5% in group with positive molecular profile. Similarly, A/G ratio reversal was seen in 83.3% patients in group with negative molecular profile and 81.3% in group with positive molecular profile.

TABLE 69C. Molecular Profile vs. Various Parameters

Serum LDH	< 225	4	13.3%	16	50.0%	20	9.526	0.003
	> 225	26	86.7%	16	50.0%	42		
Bone Marrow Aspirate / Biopsy	NORMAL	2	6.7%	1	3.1%	3	1.339	0.512
	PLASMA CELL DYSCRASIA	28	93.3%	30	93.8%	58		
	PLASMA CELL PROMINENCE	0	0.0%	1	3.1%	1		
Beta 2 microglobulin	< 3.5	6	20.0%	7	21.9%	13	0.731	0.694
	3.5-5.5	6	20.0%	9	28.1%	15		
	> 5.5	18	60.0%	16	50.0%	34		
Total		30	100.0%	32	100.0%	62		

Raised LDH levels (>225U/L) were seen in 86.7% patients in group with negative molecular profile and 50% in group with positive molecular profile. Plasma cell dyscrasia on bone marrow was seen in 93.3% patients in group with negative molecular profile and 93.8% in group with positive molecular profile. Raised beta 2 microglobulin (>5.5mg/l) was seen in 60% patients in group with negative molecular profile and 50% in group with positive molecular profile.

TABLE 69D. Molecular Profile vs. Various Parameters

		Molecular Profile										Total
		Normal		t [4:14]		t [11:14]		t [14:16]		p53 del		
MEAN	**AGE**	61.59	6.88	65.00	6.31	58.08	11.27	61.57	11.80	66.33	3.21	
Sex	F	11	37.9%	4	40.0%	8	61.5%	2	28.6%	1	33.3%	26
	M	18	62.1%	6	60.0%	5	38.5%	5	71.4%	2	66.7%	36

In our study, mean age in group of patients with t(4:14) was 65years, t(11:14) was 58.0 years, t(14:16) was 61.5, p53 del was 66.3 years. In all the groups males were more than females except the group with t(11:14) , where females (61.5%) were more than males(38.5%).

TABLE 69E. Molecular Profile vs. Various Parameters

		Molecular Profile										Total
		Normal		t [4:14]		t [11:14]		t [14:16]		p53 del		
HB gp	< 10	23	79.3%	5	50.0%	9	69.2%	6	85.7%	3	100.0%	46
TLC gp	< 4	4	13.8%	2	20.0%	0	0.0%	1	14.3%	0	0.0%	7
	4-11.0	19	65.5%	7	70.0%	11	84.6%	5	71.4%	2	66.7%	44
	> 11	6	20.7%	1	10.0%	2	15.4%	1	14.3%	1	33.3%	11
Platelet count	<1.5 Lakh	6	20.7%	4	40.0%	4	30.8%	1	14.3%	1	33.3%	16
	>1.5 Lakh	23	79.3%	6	60.0%	9	69.2%	6	85.7%	2	66.7%	46
ESR	>100	5	17.2%	1	10.0%	4	30.8%	1	14.3%	0	0.0%	11
	<50	4	13.8%	0	0.0%	2	15.4%	1	14.3%	0	0.0%	7
	50 to 100	20	69.0%	9	90.0%	7	53.8%	5	71.4%	3	100.0%	44

Anemia (Hb<10gm/dl) was seen in 50% patients with t(4:14) , 69.2% with t(11:14), 85.7% with t(14:16), 100% patients with p53 del. Leucocytosis was seen in 10% patients with t(4:14) , 15.4% with t(11:14), 14.3% patients with t(14:16), 33.3% patients with p53 del. Leucopenia was seen in 20% patients with t(4:14) and 14.3% patients with t(14:16). Thrombocytopenia was seen in 40% patients with t(4:14) , 30.8% patients with t(11:14), 14.3% patients with t(14:16), 33.3% patients with p53 del. High Esr (>50mm/hr) was seen in 90% patients with t(4:14) , 69.2% patients with t(11:14), 85.7% patients with t(14:16), 100% patients with p53 del.

TABLE 69F. Molecular Profile vs. Various Parameters

		Molecular Profile										Total
		Normal		t [4:14]		t [11:14]		t [14:16]		p53 del		
S.Creatinine	> 2	18	62.1%	6	60.0%	11	84.6%	3	42.9%	3	100.0%	41
CORRECTED CALCIUM	8.5-10.2	0	0.0%	1	10.0%	0	0.0%	0	0.0%	0	0.0%	1
	10.3-11	4	13.8%	0	0.0%	2	15.4%	2	28.6%	0	0.0%	8
	> 11	25	86.2%	9	90.0%	11	84.6%	5	71.4%	3	100.0%	53
Serum Albumin	< 3.5	19	65.5%	6	60.0%	10	76.9%	3	42.9%	2	66.7%	40
	> 3.5	10	34.5%	4	40.0%	3	23.1%	4	57.1%	1	33.3%	22
A/G RATIO	< 1.1	24	82.8%	7	70.0%	11	84.6%	6	85.7%	3	100.0%	51
	1.1-2.5	5	17.2%	3	30.0%	1	7.7%	1	14.3%	0	0.0%	10
	> 2.5	0	0.0%	0	0.0%	1	7.7%	0	0.0%	0	0.0%	1

Renal failure (serum creatinine >2mg/dl) was seen in 60% patients with t(4:14) , 84.6% with t(11:14), 42.9% with t(14:16), 100% patients with p53 del. Hypercalcemia (calcium>11mg/dl) was seen in 90% patients with t(4:14) , 84.6% with t(11:14), 71.4% with t(14:16), 100% patients with p53 del. Hypoalbuminemia (albumin<3.5gm/dl) was seen in 60% patients with t(4:14) , 76.9% with t(11:14), 42.9% with t(14:16), 66.7% patients with p53 del. Similarly, A/G ratio reversal was seen in 70% patients with t(4:14) , 84.6% with t(11:14), 85.7% with t(14:16), 100% patients with p53 del.

TABLE 69G. Molecular Profile vs. Various Parameters

		Molecular Profile										Total
		Normal		t [4:14]		t [11:14]		t [14:16]		p53 del		
Serum LDH	< 225	4	13.8%	5	50.0%	6	46.2%	4	57.1%	1	33.3%	20
	> 225	25	86.2%	5	50.0%	7	53.8%	3	42.9%	2	66.7%	42
Bone Marrow Aspirate / Biopsy	NORMAL	2	6.9%	1	10.0%	0	0.0%	0	0.0%	0	0.0%	3
	PLASMA CELL DYSCRASIA	27	93.1%	9	90.0%	12	92.3%	7	100.0%	3	100.0%	58
	PLASMA CELL PROMINENCE	0	0.0%	0	0.0%	1	7.7%	0	0.0%	0	0.0%	1
Beta 2 microglobulin	> 3.5	23	79.3%	9	90.0%	9	69.2%	5	71.4%	3	100.0%	49
Total		29	100.0%	10	100.0%	13	100.0%	7	100.0%	3	100.0%	62

Raised LDH (>225U/L) was seen in 50% patients with t(4:14) , 53.8% with t(11:14), 42.9% with t(14:16), 66.7% patients with p53 del. Plasma cell dyscrasia on bone marrow was seen in 90% patients with t(4:14) , 92.3% with t(11:14), 100% with t(14:16), 100% patients with p53 del. Raised beta 2 microglobulin (>3.5mg/l) was seen in 90% patients with t(4:14) , 69.2% with t(11:14), 71.4% with t(14:16), 100% patients with p53 del.

DISCUSSION

Multiple Myeloma is a neoplastic disease of plasma cells, which accumulate in the bone marrow and produce a monoclonal protein (immunoglobulin) usually IgG or IgA often referred to as myeloma protein. Our study was done to investigate the clinical and molecular profile of the patients at the initial presentation and also to stage them according to the revised International Staging System.

The study was conducted in the Department of Medicine, Department of Oncology and other Allied Specialties of Medicine in DMC & Hospital Ludhiana. 62 newly diagnosed cases of multiple myeloma diagnosed between 1st March 2021 and 28th Feb 2022 were included in the study from both indoor and outdoor departments of the hospital. Clinical and laboratory data of all the 62 patients was pooled together after their informed consent and was analysed. Molecular profile of all the patients was done by Fluorescence in situ hybridization method. Revised ISS staging was used and patients were classified accordingly and started on treatment.

Of the 62 patients included in our study, 36 patients (58.1%) were males and 26 patients (41.9%) were females. The male to female ratio was 1.4:1. The male preponderance observed in our study, concurs with the older study by Samuel et al[120] and by Fousad et al[112], both of which have reported male to female ratios of 1.9:1 and 1.3:1 respectively and study by Kyle et al[1] also stated male to female ratio of 1.4:1. Similarly in Asian myeloma network[106] study, male preponderance was seen with male to female ratio of 1.3:1, in study done by Kaur et al[107] male to female ratio was 1.5:1, in study by Kyle et al[1] 59% were males and 41% were females and in a study by National cancer registry[23] and Advani et al[121] male preponderance was seen with male to female ratio of 2:1 in both.

The mean age in our study was 61.6 ±8.5 years with a range of 35 years to 75 years. Samuel et al[120] in his study has reported the mean age of 61 ±7.6 years and Fousad et al[112] in his study reported mean age of 64 ± 10.7 years with the range of 39 to 83 years. In our study 4 patients (6.5%) were younger than 45 years, 7 patients (11.3%) among 46-55 year age group, 31 patients (50%) in 56-65 age group and 20 patients (32.2%) in 66-75 age group. So sixth decade was the most common age group at presentation in our study. In study conducted by Samuel et al[120] maximum patients i.e 53.8% patients were >60years and in Asian myeloma network[106] study sixth decade was the most common common age group at presentation with mean age of 62 years and an Indian study by Kaur et al[107] mean age was 58.8years with the range of 38 years to 85 years, Advani et al[121] reported mean ages of 51 years.

Fatigue and generalized weakness were the most common presenting symptoms, seen in 48 patients i.e 77.4% and weight loss and loss of appetite was seen in 33 patients (53.2%). Bone pain was the main presenting complaint in 32 patients (51.6%). Approximately one third to two third patients of multiple myeloma present with the complaint of bone pain because of vertebral collapse, osteopenia or fractures. Similar results were seen in a study done by Chowdhury et al[113] wherein most common presenting complaint was fatigue and weakness in 87.5% patients, bone pain in 80% patients and fever in 31.2% of the patients. Similarly in a study done by Fousad et al[112] the most common symptom was fatigue (100%) and bone pain (96.9%). In study by Kyle et al[1], bone pain was the main presenting complaints in 58% patients, fatigue in 32% patients, and weight loss in 24%. In study by Kaur et al[107], bone pain was the most common presenting complaint in 50% patients, followed by fatigue and generalised weakness in 46.4% patients. In study done by Gupta et al[122] also bone pain was the most common complaint followed by fatigue and generalised weakness. In study by Subramanian et al.[123], easy fatiguability and bone pain were the most common presenting complaints.

Fever was present in 26 patients (41.9%), similar to study by Chowdhury et al[113] (31.2%) and Diwan et al[108] (35%). Majority of the patients in our study had documented focus of infection, 16 had pneumonia and 6 patients had UTI. Mai-Yu-Jie et al[124] reported fever in 20% patients in a study done on 532 patients. Kyle et al[1] reported fever as a main presenting complaint only in 0.7% patients. Thus fever as a main presenting complaint is more common in our study which could be explained due to more patients presenting late after acquiring infections as compared to the patients in the developed countries.

Other less common presenting complaints were dyspnea (seen in 30.6% of the patients), decreased urine output (seen in 25.8% of the patients) and altered sensorium (seen in 3.2% of the patients). Altered sensorium was due to hypercalcemia and renal failure. No patient was found to have neuropathy. In a study done by Walsh[125], clinical evidence of neuropathy was reported in 30% patients and in a study done by Kyle et al[1], parasthesias were recorded in 5% and Kelly E. Dooley[126] reported clinical polyneuropathies in 13% of newly diagnosed myeloma cases. In study conducted by Samuel et al[120], 7.7% patients had neurological manifestations.

Bleeding was seen in 2 patients, both of whom had thrombocytopenia and had gastrointestinal bleed. Mai-Yu-Jie et al[124] in his study reported bleeding in 23.4% patients and major cause was hyperviscosity followed by thrombocytopenia and main site of bleeding was gastrointestinal followed by urinary tract.

14 out of 62 patients (22.6%) were diabetic, 11 patients (17.7%) were hypertensive and 2 patients (3.2%) had h/o coronary artery disease. The data was comparable to the study by Fousad et al[112], in which 25% patients had a history of diabetes mellitus and systemic hypertension.

On examination, the most common finding was pallor, seen in 50 out of 62 patients (80.6%), followed by edema feet seen in 5 patients (8%). In study

conducted by Samuel et al[120], the most common clinical sign was pallor (92.3%), followed by edema feet (40%). In a study by Fousad et al[112], pallor was the most common finding (90.6%), along with spine tenderness (90.6%), followed by edema (53.1%). No organomegaly or lymphadenopathy was found in our study.

Hemoglobin values in our patients ranged from 4.0- 12.2gm/dl. Mean Hb in our study was 8.5gm/dl. 46 out of 62 patients had Hb <10gm/dl (74.2%) and 38.7% patients had Hb <8gm/dl. In study by Samuel et al[120], Hb<10gm/dl was seen in 69.2% with the mean Hb of 8.6g/dl. In a study done by Chowdhury et al[113] anemia was seen in 62.5% patients. In a study by Kaur et al[107] Hb<10gm/dl was seen in 92.8% of the patients with range of 2.1-10.5gm/dl. On the contrary in a study by Kyle et al[1] anemia was found only in 35% of the patients. In a study by Asian myeloma network[106], Hb<10gm/dl was seen in 60.7% of the patients. In study by Fousad et al[112] it was found in 50% of the patients.

The anemia observed was normocytic normochromic in 67.7% patients and microcytic hypochromic in 32.3% patients, similar to as reported in literature (Dispenzieri et al[19]). Anemia is a significant finding in multiple myeloma which occurs due to either erythropoietin deficiency or marrow infiltration by myeloma cells or from accompanying renal failure. Anemia has been shown to be a poor prognostic factor in multiple myeloma.

Leucopenia was seen in 11.3% patients while majority of the patients (71% patients) had TLC count within normal range (4-11x $10^3/mm^3$). Leucocytosis (TLC >11x $10^3/mm^3$) was seen in 17.7% of the patients. In a study done by Chowdhury et al[113], 71.9% patients had normal TLC count, 15.6% had leucopenia and 12.5% patients had leucocytosis. In study done by Fousad et al[112] 90.6% patients had normal TLC count, only 3.1% had leucopenia and 6.3% patients had leucocytosis. In study by Kyle et al[1], 20% patients had leucopenia, majority of the pateints had normal TLC count (72%) and 8%

patients had leucocytosis. Leucopenia is predominantly due to bone marrow infiltration with plasma cells and is more common in advanced stages of myeloma with high tumor load. Leucocytosis is usually associated with leukemoid reaction, myeloproliferative disorder, and chronic lymphocytic leukemia.

Thrombocytopenia (platelet count <1.5 lakh/mm^3) was seen in 16 patients (25.8%), rest of the patients had platelet count of >1.5lakh/mm^3. Thrombocytopenia is frequently observed in multiple myeloma and could be due to infiltration of the marrow by plasma cells, infection or intravascular destruction of platelets. This is similar to the study done by Kaur et al[107] 25% patients had thrombocytopenia and in study done by Fousad et al[112] thrombocytopenia was seen in 15.6% patients. In a study done by Chowdhury et al[113], 18.7% of the patients had thrombocytopenia.

Prominent Rouleaux formation was seen in 38 patients (61.3%). In study done by Kyle et al[1], it was seen in 56% patients, and similar results were observed in previous studies. On the contrary rouleaux formation was seen in 82% patients in a study done by Kaur et al[107]. Probable reason of this difference could be difference in sample size (62 patients in our study vs. 28 in their study).

None of the patient in our study had normal ESR, 55 out of 62 patients (88.7%) had ESR >50mm/hour with a mean ESR of 78.6mm/hr. In study done by Fousad et al[112] all the patients had elevated ESR (100%). In study done by Kyle et al[1], ESR was > 20mm/hr in 84% of the patients and >100mm/hr in one third of the patients. Raised ESR is attributed to increased serum proteins, inflammatory state and anemia seen in patients with multiple myeloma.

Serum protein electrophoresis is an easy, inexpensive method of separating proteins based on their net charge, size and shape. M protein is usually a single narrow peak that is composed of a single class of

immunoglobulins secreted by abnormally expanded clone of plasma cells, in gamma, beta or alpha 2 regions. 58 out of 62 patients (93.5%) had M spike on serum protein electrophoresis. In study done by Fousad et al[112] M spike on serum protein electrophoresis was seen in 94% of the patients. In study done by Kyle et al[1], it was seen in 93% of the patients. So, 4 patients had no M spike, so they were designated as having non secretory myeloma.

Hypercalcemia is one the important diagnostic marker for multiple myeloma (CRAB criteria). Corrected calcium measured in all the patients ranged from 10.2mg/dl to 16.8mg/dl with a mean value of 12.6±1.4mg/dl.. Hypercalcemia, according to IMWG criteria defined as calcium >11mg/dl, was seen in 53 out of 62 patients (85.5%). In a study done by Kaur et al[107], it was seen in 46% patients and in a study done by Samuel et al[120], it was seen in 44.6% of the patients. In a study by Sultan et al[29] it was in 40.9% patients and in study by Asian myeloma network[3], hypercalcemia was seen in 16.7% patients. In a study by Fousad et al[112], hypercalcemia was seen in 18.8% patients and in a study by Kyle et al[1] it was seen in 13%. The higher incidence of hypercalcemia in our study can be explained by the fact that most of the patients presented in stage III disease with high tumor burden, with concomitant renal failure.

Serum creatinine in our study ranged from 0.6mg/dl to 9.8mg/dl with a mean of 2.9±1.7mg/dl. Renal failure with creatinine of >2mg/dl was observed in 41 out of 62 patients (66.1%) with a mean creatinine of 2.9mg/dl. Serum creatinine values ranged from 0.6 – 9.8mg/dl. Study by Kyle et al[1] showed renal impairment in 55% patients and study by Kaur et al[107] showed renal impairment (>2mg/dl) in 86.4% patients. In study by Samuel et al[120] renal impairment was seen in 43.1% and in a study by Fousad et al[112], it was seen in 21% patients. In a study by Asian myeloma network[106], renal impairment (creatinine >2mg/dl) was seen in 23.4% patients. Approximately, 30-86% myeloma patients in India have renal

failure at the time of diagnosis[108,131] which is much higher as compared to the western world. The probable reason could be late presentation and lack of early screening resources. Renal failure in myeloma is mainly due to myeloma nephropathy (i.e precipitation of monoclonal light chains in the kidneys), hypercalcemia, hyperuricemia or dehydration.

Bony abnormalities were found in 55 out of 62 patients (88.7%). Lytic lesions were found in 37 patients (59.7%).The most common site of bony lytic lesion was the skull. 7 patients had diffuse osteopenias (11.3%). 8 patients had fractures (12.9%) and 3 patients (4.8%) had vertebral wedge collapse on skeletal survey. In a study done by Chowdhury et al[7], bony abnormalities were found in 87.5% patients, out of which 53.1% had lytic lesion, 21.8% had vertebral compression fracture and 12.5% had osteoporosis, Lytic bone lesions were seen in 80% of the patients in a study by Kaur et al[107], whereas it was seen in 62% patients in study by Prakash et al[131]. In study by Fousad et al[112], it was seen in 90.6% patients. The most common site was skull in all the studies. In a study by Asian myeloma network[106], bone lesions were seen in 60.2% of the patients. In a study by Kyle et al[1], bony abnormalities were seen in 79% of the patients with lytic lesions in about 67% of the patients and 20% had osteoporosis, pathologic fractures, compression fractures, or osteopenia.

Beta 2 microglobulin is a important prognostic marker and an important parameter in revised ISS. The human leucocyte antigen complex extends over 4000 kilo bases on the short arm of chromocome 6 and is divided into three regions class I, II and III. The class I molecule is a heterodimer that consists of an H chain and a non covalently associated light chain that is known as Beta 2 microglobulin. It is present on all cells and its synthesis is increased in multiple myeloma. Raised serum beta 2 microglobulin levels i.e >3.5mg/dl, is a poor prognostic marker, which was seen in 49 out of 62 patients (79%) with a mean value of 7.2± 5.3. In a study done by Chowdhury et al[113], raised serum beta 2 microglobulin

levels i.e >3.5mg/dl were seen in 84.4% of the patients. In a study by Kaur et al[107] raised serum beta 2 microglobulin levels were seen in 71.4% of the patients, with 75% patients in a study by Kyle et al[1], and 65.5% patients in a study by Asian myeloma network[106].

Serum albumin levels of the patients in our study group ranged from minimum value of 1.8gm/dl to maximum value of 3.8gm/dl with mean value of 3 ± 0.6gm/dl. Low serum albumin (serum albumin<3.5gm/dl) is also a poor prognostic marker, which was seen in 35 patients (56.5%) similar to study done by Lee et al[106] in which it was seen in 52% of the patients. In study done by Asian myeloma network[106] low albumin level was seen in 52% of the patients, and in study by Fousad et al[112] low serum albumin was seen in 62.5%. Low serum albumin is thought to be mediated by the effects of inflammatory cytokines like IL-6.

In our study, 44 out of 62 patients (70.9%) had serum total proteins from 6 to 9 gm/dl and 10 patients out of 62(16.2%) had total protein from 4 to 6 gm/dl and 8 patients out of 62 had serum total proteins of >9gm/dl(12.9%).45 patients (72.6%)had increased serum globulins >3.5gm/dl, 15 patients(24.2%) had normal globulins(2-3.5g/dl), 2 patients(3.2%) had low levels of serum globulins (<2gm/dl). So, A/G ratio reversal was seen in 51 out of 62 patients (82.3%), similar to study done by Samuel et al[120] in which it was seen in 84.6% patients.

Bone marrow study done in our study revealed plasma cell dyscrasia seen in 58 out of 62 patients (93.6%) i.e with plasma cells >10% with or without plasmbablastic morphology. Plasma cells >30% were seen in 38.7% of the patients. Similarly, study by Samuel et al[120] and study by Kim et al[106] revealed plasma cells >30% in 36.9% and 48.4% respectively. In study done by Kyle et al[1], similar results were obtained as 96 % of the patients had bone marrow with 10% or more plasma cells. In a study done by

Tanvi sood et al[127], 90.9% patients had plasmacytosis >10% on bone marrow examination. In study by Fousad et al[112], 75.1% patients had bone marrow with 10% or more plasma cells.

Serum LDH is a simple, readily available and inexpensive test which helps in identifying subsets of patients with poor outcome. It is one of the main marker for staging (revised ISS) multiple myeloma. Serum LDH levels in our study ranged from a minimum value of 106 to maximum value of 826 with a mean value of 394±199.8U/Land it was raised in 42 out of 62 patients (67.7.%). It is one of the important prognostic markers and part of the revised ISS staging of multiple myeloma. In a study done by Kaur et al[107], raised serum LDH was found in 78.5% of the patients, this difference can due to the small sample size of the study and the stage at which patient presents to the hospital.

Serum Immunofixation study is used with serum electrophoresis to determine the type and amount of monoclonal protein (M-protein, or paraprotein) present in a patient with a suspected plasma cell disorder. Immunofixation electrophoresis (IFE) is performed by separating plasma proteins by electrophoresis, followed by addition of specific antisera against each type of immunoglobulin. On serum immunofixation , 13 out of 62 patients had IgA kappa monoclonal gammopathy (21.0%), 1 patient had IgA lambda monoclonal gammopathy (1.6%), 20 patients had IgG lambda monoclonal gammopathy (32.3%), 27 patients had IgG kappa monoclonal gammopathy (43.5%), and 1 patient had normal serum immunofixation (1.6%). So the most common type of myeloma in our study was IgG KAPPA, as seen in studies by Samuel et al[120], Asian myeloma network[106] and Kyle et al[1]. Involved light chain was kappa in 64.5% and lambda in 33.9% patients. Similarly, involved heavy chains

include IgG in 75.8% and IgA in 22.6% patients. In a study by N. H.Abdallah.et al[129], kappa in 65% and lambda in 35% patients.

TABLE 70: Studies on serum immunofixation

TYPE	Our study	Kyle et al	AnilTarigopula et al
IgG KAPPA	43.5%	34%	22.2%
IgG LAMBDA	32.3%	18%	46.3%
IgA KAPPA	21%	13%	13%
IgA LAMBDA	1.6%	8%	18.5%

A variety of chromosomal alterations have been found in patients with myeloma: hyperdiploidy, 13q14 deletions, translocations t [11:14], t [14:16], t [4:14], 1q amplification or 1 p deletion, deletion 17p13. Molecular Profile panel done in our institute includes the translocations -t[11:14], t[14:16], t[4:14],and deletion - del 17p13 [p53]. Molecular profile panel done in all 62 patients revealed 33 out of 62 patients (53.2%) had positive molecular profile, with most common being t[11;14] in 13(20.9%) patients , followed by t[4;14] in 10 patients(16.1%), t[14;16] in 7 patients (11.2%) and p53 deletion in 3 patients (4.8%).In study done by Asia myeloma network[106] t[11;14] was seen in 17.4% patients, followed by t[4;14] in 10.5% patients, t[14;16] in 4.4% patients and p53 deletion in 13.3% patients. In study done by Kumar et al[132] t[11;14] was seen in 18%

patients , followed by t[4;14] in 10% patients, t[14;16] in 5% patients and p53 deletion in 13% patients. In study done by Anil Tarigopula et al[128] t [11; 14] was seen in 7.7% patients, t[4;14] in 21% patients, t[14;16] in 4.4% patients and p53 deletion in 7.7% patients. In study done by N. H. Abdallah et al[129], similar results were seen as t[11;14] was seen in 21% patients , followed by t[4;14] in 10% patients, t[14;16] in 4% patients and p53 deletion in 13% patients.

Staging was done as per the revised ISS, 28 out of 62 patients (45.2%) were in stage II and 34 patients (54.8%) in stage III, however no patient presented to us in stage I. Palumbo et al[130] did an international trial on 3060 patients, as per revised ISS, 28%patients were in stage I, 62% patients in stage II and only 10 % patients in stage III.

In a study by Victor H. Jimenez-Zepeda et al [133], out of 381 patients 20% were classified in stage I, 67.5% in stage II and 12.6% in stage III. In a study by N.Tandon et al[134], out of 1352 patients 17%(229) were classified in stage I, 69.4%(938) in stage II and 13.7%(185) in stage III. In a study by N.H. Abdallah et al[129]. 36% patients in stage I, 33% in stage II, and 31% in stage III. However, this could be due to small sample size in our study and due to late presentation of the patients to the health care centres in our country especially north India due to lack of knowledge and scarcity of resources and financial constraints.

Out of 62 patients in our study, 56 patients were indoor patients and 6 patients were treated on Opd basis and out of 56 admitted patients 3 patients died during their hospital course while rest all were alive. All 62 patients were started on induction therapy with various regimens as follows- 26 patients (41.9%) were started on Bortezomib, Dexamethasone and Lenalidomide regimen, 14 patients(22.6%) started on Bortezomib, Dexamethasone and Cyclophosphamide regimen, 11 patients(17.8%)

started on Bortezomib, Dexamethasone and Thalidomide regimen, 8 patients(12.9%) started on Dexamethasone and Bortezomib regimen, 3 patients (4.8%) started on Dexamethasone and Thalidomide regimen. In study done by Fousad et al[112], 40.6% received Cyclophosphamide, Dexamethasone and Thalidomide regimen, 9.4% received Bortezomib, Dexamethasone and Thalidomide, 6.3% received Bortezomib, Cyclophosphamide and Thalidomide, 15.6% received Dexamethasone and Thalidomide regimen. In a study by Victor H. Jimenez-Zepeda et al[133], 31.6% patients were started on Bortezomib, Dexamethasone and Cyclophosphamide regimen, 28.6% patients on Dexamethasone and Bortezomib regimen, 10.9% patients on Bortezomib, Dexamethasone and Lenalidomide regimen, 10.1% patients on Vincristine, Doxorubicin, and Dexamethasone.

Similarily in study by Asian myeloma network[106], newer drugs such as bortezomib, lenalidomide were used in 36% patients. Cowan et al[135] in his study started all the patients on induction therapy with Bortezomib, Dexamethasone and Lenalidomide. And this induction therapy combined with autologous hematopoietic stem cell transplantation followed by maintenance lenalidomide as the standard of care for eligible patients. Similarly all the updates on treatment of myeloma with high risk cytogenetics, state Bortezomib, Dexamethasone and Lenalidomide as first line therapy along with autologous hematopoietic stem cell transplantation (in eligible patients).

The various parameters like age, sex, hematological, biochemical and cytogenetic markers were correlated with the revised international staging system (R-ISS).

There was no significant difference in the male to female ratio among the patients in stage II and stage III groups. Also, there was no significant

difference in the percentage of the patients in various age groups on comparison among the stage II and stage III patients. In our study, anemia (Hb<10gm/dl) was found to be more common in stage III patients i.e 30 out of 34 patients (88.2%) vs. 16 out of 28 patients(57.1%) in stage II, with a significant p value of 0.001. Rouleaux formation was found in 64.7% of the patients in stage III vs. 57.1% patients in stage II. However it was not statistically significant. In our study, total leucocyte count (leucopenia, normal TLC, leucocytosis) was similar in stage II and stage III groups. Thrombocytopenia was found to be more common in stage III i.e 32.4% patients vs. 17.95 patients in stage II (p value – 0.051).

On comparision of ESR among stage II and stage III groups, it was found that ESR was high in similar percentage of patients in stage II and stage III groups. Serum calcium of >11mg/dl was found in 88.2% of the patients in stage III and 82.1% of the patients in stage II disease (p value – 0.507, not statistically significant). Similarly, renal failure (serum creatinine >2mg/dl) was observed in 70.6% in stage III and 60.7% in stage II, but had no statistically significant correlation (p value – 0.414). Serum albumin of < 3.5gm/dl was found in 30 out of 34 patients (88.2%) in stage III vs. 5 out of 28 patients (17.9%) in stage II, thus having a stastically significant (p value of 0.00) correlation with the staging of the disease. A/G ratio reversal was seen in 91.2% of the patients in stage III vs. 71.4% of the patients in stage II (p value - 0.109).

There was no difference in alkaline phosphatase values in stage II and stage III disease. Similarly, there was no statistical difference in the percentage of fractures in stage III and stage II disease i.e 8.8% vs 17.9% respectively (p value 0.291). However on comparing alkaline phosphatase levels with fractures on skeletal survey, significant correlation of raised alkaline phosphatase with fractures was seen, as out of all the 8 patients with fractures in our study, 7 patients had raised alkaline phosphatase

levels, while only 1 patient out of the rest 54 patients had raised alkaline phosphates (p value-0.001). Raised serum LDH level was found in all the 34 patients of stage III (100%) vs. 20 out of 28 patients (71.4%) in stage II, which was statistically significant.

On comparing various translocations, 16 out of 28 patients (57.1%) in stage II disease vs. 17 out of 34 patients (50%) in stage III disease (p value 0.933). So, t(4:14) was found in17.9% of the patients in stage II vs. 14.7% of the patients in stage III, t(11:14) was found in 21.4% of the patients in stage II and 20.6% of the patients in stage III, t(14:16) was found in 14.3% of the patients stage II and 8.8% of the patients in stage III, p53 del was found in 3.6% patients in stage II and 5.9% of the patients in stage III. On bone marrow examination, plasma cell dyscrasias (plasma cells>10% with / without plasmablastic morphology) was found in 92.9% of the patients in stage II and 94.1% of the patients in stage III.

So, our study revealed significant statistical correlation of staging with anemia, raised serum beta 2 microglobin, raised serum LDH, low albumin, thrombocytopenia. But higher percentage of patients had hypercalcemia, anemia and majority of patients presented in stage III, could be due to late presentation of patients to a tertiary care hospital.

In a study done by Noorjahan Mohammed et al[117] , on comparing various biochemical parameters with different stages of multiple myeloma, it was found that serum creatinine, serum calcium, serum beta 2 microglobulin, hemoglobin, serum albumin and M protein had significant correlation with the stages (p value<0.05). In a study done by Chethana Babu K Udupa et al[136], correlation between revised ISS stages and molecular cytogenetics was done which was statistically insignificant (p value-0.213).

In our study, it was found that 59 out of 62 patients (95.2%) got discharged or had done so against medical advice (DAMA), while 3 patients (4.8%) died while being treated in the hospital.

The various parameters like age, sex, hematological, biochemical and cytogenetic markers were compared with the outcome of the patient (death vs. discharge/ DAMA).

In our study, all the 3 patients (100.0%) who died were in the age group of 56 to 65 years and 28 out of 59 patients (47.5%) who got discharged/ DAMA were also in the age group 56 to 65 year. Anemia (Hb <10gm/dl) was seen in 2 out of 3 patients (66.7%) who died vs 50 out of 59 (84.7%) patients who got discharged/ DAMA. Raised ESR (>100mm/hr) was seen in 2 out of 3 patients (66.7%) who died vs 53 out of 59 patients (89.8%) who got discharged/ DAMA. Thrombocytopenia (PLT<1.5lakh/mm^3) was seen in 1 out of 3 patients (33.3%) who died vs 15 out of 59 patients (25.4%) who got discharged/ DAMA. Total leucocyte count was within normal range among all the 3 patients (100%) who died whereas 11.9% patients who got discharged/ DAMA had leucopenia and 18.9% patients had leucocytosis.

Renal failure (serum creatinine >2mg/dl) was found in 2 out of 3 patients (66.7%) who died vs 39 out of 59 patients (66.1%) who got discharged/ DAMA. Hypercalcemia (serum calcium >11mg/dl) was seen in 2 out of 3 patients (66.7%) who died vs 51 out of 59 patients (86.4%) who got discharged/ DAMA. High LDH (>225 IU/L) was seen in all the 3 patients who died (100%) vs 39 out of 59 patients (66.1%) who got discharged/ DAMA. Hypoalbuminemia (serum albumin<3.5gm/dl) was seen in 2 out of 3 patients (66.7%) who died vs 33 out of 59 patients (55.9%) who got discharged/ DAMA. Beta 2 micro globulin was >5.5 mg/l in 2 out of 3 patients (66.7%) who died vs 32 out of 59 patients (54.2%) who got discharged/ DAMA.

Plasma cell dyscrasia (plasma cells >10% with or without plamsablastic morphology) was found in all 3 patients who died (100%) and 55 out of 59 patients (93.2%) who got discharged/ DAMA on bone marrow examination.. In our study, positive molecular profile was seen in 31 of 59 patients (52.5%) and 2 out 3 patients (66.7%) who died.

The various demographic and biochemical parameters like age, sex, hemoglobin, creatinine, beta 2 microglobulin etc. were compared among the patients with positive molecular profile vs. those with the negative molecular profile.

The mean age , male to female ratio, anemia, thrombocytopenia, TLC and ESR were not significantly different between both the groups.Similarly, there was no difference observed in renal failure, hypercalcemia , albumin, A/G ratio, plasma cell dyscrasia and beta 2 microglobulin among both the groups.

So further, the parameters were compared among the molecular profile groups which were t(4:14), t(11:14), t(14:16) and p53 deletion. In our study, the mean age of the patients was >60 years in all the groups except those with t (11:14) in which the mean age was 58 years i.e. <60 years. In all the groups, there was male preponderance except in group with t(11:14) where the incidence was more in females (61.5%) vs. males (38.5%).Anemia (Hb<10gm/dl) was more commonly observed in patients with p53 del (100%) and t(14:16) (85.7%). Leucopenia was seen in 20% patients with t(4:14) and 14.3% patients with t(14:16) whereas leucocytosis was more common in p53 del (33.3%). Thrombocytopenia (platelet count <1.5 lakh/mm^3) was least common in patients with t(14:16). High ESR was seen in all the groups, least common in t (11:14).

Renal failure (serum creatinine >2mg/dl) was more common in patients with p53 del (100%) and t (11:14) (84.6%). Hypercalcemia (Serum calcium >11mg/dl) was seen commonly among all the groups but was least common among patients with t(14:16)(71.4%). Hypoalbuminemia (S.

albumin<3.5mg/dl) was observed in all the groups and so was A/G reversal with highest percentage in group with p53 del (100%). Raised LDH (>225U/L) and Plasma cell dyscrasia was seen in all the groups with molecular profile positive. Raised beta 2 microglobulin (>5.5mg/l) was seen in all the groups but was more common in p53 del (100%) and t(4:14) (90%).

In a study done by Abdallah N et al[129], the most common translocation was t(11:14) similar to our study and translocations- t(4:14), t(14:16), t(6:14) and t(14:20) were associated with anemia, raised beta 2 microglobulin (>5.5mg/l), >50% bone marrow plasma cells. In a study done by Anil Tarigopula[8], the most common translocation was t(11:14) similar to our study and t(11:14), t(4:14), t(14:16) were associated with anemia, renal failure, hypercalcemia, low albumin and raised beta 2 microglobulin as observed in our study.

Thus, our study showed that multiple myeloma is a disease of middle and elderly aged population with male preponderance, with high male female ratio. The percentage of various parameters like age, male to female ratio, clinical presentation, lab parameters like serum creatinine, TLC, thrombocytopenia, albumin, serum LDH, beta 2 microglobulin and the molecular profile were comparable to the other studies. However, a higher percentage of patients had hypercalcemia in our study. Majority of patients presented in stage III. This corresponds with higher tumor cell burden and could be due to smaller size of our study group or due to late presentation of patients to our tertiary care hospital. Molecular profile , which was positive in 53.2% of the patients, revealed t(11:14) was the most common followed by t(4:14), t(14:16) and then p53 del. To conclude our study showed that, investigativel workup of multiple myeloma patients should include beta 2 microglobulin, serum LDH, and molecular profile in addition to the routine workup of the patients to appropriately stage the disease and plan the treatment for an optimal outcome.

SUMMARY & CONCLUSION

Summary

- The study was conducted in the Department of Medicine, Department of Oncology and other Allied Specialties of Medicine in DMC & Hospital Ludhiana. 62 newly diagnosed cases of multiple myeloma diagnosed between 1st March 2021 and 28th Feb 2022 were included in the study from bothindoor and outdoor departments of the hospital
- Bone marrow examination, serum protein electrophoresis, and a molecular profile were among the common laboratory tests documented.
- Patients were diagnosed according to the IMWG criteria of multiple myeloma.
- 36 males and 26 females were newly diagnosed as MM patients.
- Maximum number of patients i.e 50% were between 56-65 years, followed by 32.2% in 66-75 years. Mean age at the diagnosis was 61.6years.
- Major presenting complaint was fatigue and generalized weakness, followed by weight loss, bone pain, dyspnea and fever. 12 patients had type 2 diabetes mellitus, 9 patients had hypertension, 2 patients had both diabetes mellitus type 2 and hypertension, 2 patients had h/o coronary artery disease.
- All the patients except 1 had anemia at the time of diagnosis, with forty six patients having Hb<10gm/dl. The mean Hb was 8.5gm/dl.
- Leucopenia was seen in 7 patients and leucocytosis was seen in 11 patients. Most common infection seen in our patients was lower respiratory tract infection followed by urinary tract infection.
- 16 patients had thrombocytopenia at the time of diagnosi and 2 out of them had gastrointestinal bleed.
- ESR was raised in all patients with a mean ESR of 78.6mm/hr.

- 41 patients in our study had renal failure, with a mean creatinine of 2.9mg/dl.
- Hypercalcemia was seen in 53 out of 62 patients with mean calcium of 12.6mg/dl.
- Beta 2 microglobulin >5.5mg/l was seen in 34 patients (with a mean of 7.2mg/l) and all of them presented in stage III according to R-ISS.
- Raised serum LDH was seen in 42 patients and 34 out of those who presented in stage III .
- 33 patients had positive molecular profile, including thirteen cases of t(11:14), ten cases of t(4:14), seven cases of t(14:16), and three cases of p53del.
- According to R-ISS staging, 28 patients were in stage II and 34 patients were in stage III at the time of presentation.
- It was also found that there is significant statistical correlation of anemia, hypoalbuminemia, raised serum LDH, thrombocytopenia and raised beta 2 microglobulin levels with the staging of the disease.
- The mean age, male to female ratio, anemia, thrombocytopenia, albumin , beta 2 microglobulin and plasma cell dyscrasia were not found to be different between the patients with molecular profile positive and negative.

Conclusion

Diagnosis of multiple myeloma is being made more frequently now-a-days because of easier and wider availability of the various investigations. Myeloma should be considered in any patient above 50 years of age who presents with undiagnosed anemia, bone pains or renal failure.

This study showed that multiple myeloma is a disease of middle and elderly aged population with male preponderance, with high male female ratio. The percentage of various parameters like age, male to female ratio, clinical presentation and lab parameters like serum creatinine, hemoglobin, albumin, serum LDH, beta 2 microglobulin and the molecular profile weremcomparable to the other studies. However, a higher percentage of patients had hypercalcemia, anemia and majority of patients presented in stage III. This corresponds with higher tumor cell burden and could be due to smaller size of our study group or due to late presentation of patients to our tertiary care hospital. Molecular profile of the patients revealed t(11:14) was the most common followed by t(4:14), t(14:16) and then p53 del. Investigational workup of multiple myeloma patients should include beta 2 microglobulin, serum LDH, and molecular profile in addition to the routine workup of the patients to appropriately stage the disease and plan the treatment for an optimal outcome.

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PROFORMA

Sr No.

Name

Mrd No.

Age/ Sex:

Father's Name

Address

Occupation

Date of Admission

Date of Discharge

Presenting Complaints And Duration

- Bony Pains
- Fractures
- Fatigue
- Dyspnea
- Weight Loss/Loss Of Appetite
- Decreased Urine Output
- Altered Sensorium
- Fever
- Any Other Complaints

Date of Diagnosis

Comorbid Illness

Signature of Candidate

Signature of Supervisor

EXAMINATION

GENERAL EXAMINATION

ECOG PS

BMI

Pulse Rate
Blood Pressure
Respiratory Rate
Cyanosis

Clubbing
Icterus
Pallor
JVP

SYSTEMIC EXAMINATION

1. Respiratory System

2. Abdomen

3. Cardiovascular System

4. Central Nervous System

Signature of Candidate **Signature of Supervisor**

INVESTIGATIONS

HB

PCV

Platelet count

ESR

TLC

DLC

PBF

Blood Urea

S.Creatinine

S.Bilirubin

SGOT/SGPT

Alkaline Phosphatase

S.Phosphate

Corrected Calcium

Serum Albumin

Serum Total Protein

Serum LDH

Blood Sugar

Serum Protein Electrophoresis

Serum Immunofixation [if indicated]

Serum Free Light Chain Assay [if indicated]

Signature of Candidate **Signature of Supervisor**

Bone Marrow Aspirate / Biopsy

Skeletal Survey/ PET-CT Scan

Viral markers [if indicated]

Beta 2 microglobulin [if indicated]

Molecular Profile -

t [4:14]

t [11:14]

t [14:16]

p53 del [17p13 del]

Stage

Final Diagnosis

Outcome –

INDOOR – Discharge / Dama / Death

Treatment Started – Yes / No

OUTDOOR – Treatment Started – Yes / No

Treatment Plan / Given:

Signature of Candidate **Signature of Supervisor**

				Presenting Complaints And Duration									GENERAL EXAMINATION													
Sr. No	Mrd No	Age	Sex	BONY PAINS	FRACTURES	FATIGUE	DYSPNEA	WEIGHT LOSSS/ LOSS OF APPETITE	DECREASED URINE OUTPUT	ALTERED SENSORIUM	FEVER	ANY OTHER COMPLAINTS	ECOG PS	BMI	EDEMA	Icterus	Pallor	hepatomegaly/ splenomegaly	motor/ sensory loss	HB	HB	PCV	Platelet count	ESR	TLC	PBF	PBF
1	1031945	64	M	-	-	YES	YES	YES	-	-	-	COUGH	-	21	-	-	+	-	-	8 to 10	9.8	32	148000	140	8	1	RF +
2	1184245	74	M	YES	-	YES	-	YES	-	-	-	-	-	24	-	-	+	-	-	<8	6.1	21	124000	125	8.3	1	RF +
3	1183832	49	M	-	-	YES	-	-	YES	-	-	-	-	26	+	-	+	-	-	8 to 10	8.6	24.2	200000	80	1.1	0	RF-
4	1018698	65	F	YES	-	-	-	-	-	-	YES	-	-	23.4	-	-	+	-	-	<8	7.8	23	229000	92	6.4	1	RF +
5	1101912	49	M	YES	-	YES	-	YES	-	-	YES	-	-	27	+	-	+	-	-	<8	5	17	188000	48	4.8	0	RF-
6	978408	74	M	YES	-	YES	ES	YES	-	-	-	-	-	22	-	-	-	-	-	8 to 10	8.5	38	190000	67	2.1	0	RF-
7	1133901	60	F	-	-	YES	YES	YES	-	-	-	-	-	26	-	-	+	-	-	8 to 10	8.6	34	316000	47	8.1	1	RF +
8	1139420	62	M	YES	YES	YES	YES	-	-	-	-	-	-	23	-	-	+	-	-	<8	6.8	33	159000	42	10.7	1	RF +
9	1135109	70	M	YES	-	YES	YES	-	-	-	YES	-	-	30.8	-	-	+	-	-	<8	6.2	21	98000	62	7	2	TCP
10	1001216	54	M	-	YES	YES	-	YES	-	-	YES	-	-	28	-	-	-	-	-	8 to 10	9.8	27	154000	69	4.8	0	RF-
11	1060931	60	F	-	-	YES	-	YES	-	-	-	-	-	27.4	-	-	+	-	-	8 to 10	9.4	36	195000	64	16.6	0	RF-
12	1080830	42	M	YES	YES	YES	-	-	-	-	YES	-	-	27.4	-	-	+	-	-	8 to 10	9	26	152000	82	9.5	1	RF +
13	363606	64	M	YES	-	YES	-	-	YES	-	-	-	-	23.7	+	-	+	-	-	8 to 10	8.6	28	108000	80	4.4	0	RF-
14	1033593	65	F	-	-	YES	YES	-	YES	YES	-	GI BLEED	-	23.4	-	-	+	-	-	<8	5.5	16	48000	120	7.5	1	RF +
15	782448	50	M	-	-	YES	-	YES	-	-	-	-	-	26.5	-	-	-	-	-	>10	11	24	215000	102	5.6	1	RF +
16	1024015	40	F	YES	-	-	YES	YES	-	-	-	-	-	24.3	-	-	+	-	-	8 to 10	9.5	31	199000	70	7.8	0	RF-
17	1087788	61	F	YES	-	YES	-	YES	-	-	-	-	-	21	-	-	+	-	-	<8	7.8	25.6	388000	120	19	1	RF +
18	1087788	60	F	YES	-	YES	-	YES	-	-	-	-	-	25	-	-	+	-	-	8 to 10	8.8	28	360000	114	15.8	0	RF-
19	1017605	61	M	YES	-	YES	-	-	-	-	YES	-	-	27.8	-	-	-	-	-	>10	12	34	90000	90	4.8	1	RF +
20	1263040	35	F	-	-	YES	-	YES	YES	YES	YES	GI BLEED	-	19	-	-	+	-	-	>10	10.2	30	34000	28	9.4	0	RF-
21	1185496	57	M	-	-	-	-	YES	-	-	YES	-	-	24	-	-	+	-	-	<8	5.2	24	154000	78	3.8	0	RF-
22	1183712	66	F	-	-	YES	-	-	-	-	YES	-	-	28.4	-	-	+	-	-	8 to 10	8.1	20.4	281000	78	7.6	1	RF +
23	1271610	60	F	YES	-	YES	-	-	-	-	-	-	-	26	-	-	+	-	-	<8	4	24	66000	112	4.8	1	RF +
24	975155	57	F	YES	-	YES	-	YES	-	-	-	-	-	27	-	-	+	-	-	<8	6	21	110000	76	2.9	1	RF +
25	1218881	64	M	-	-	YES	-	YES	YES	-	YES	-	-	28	-	-	+	-	-	8 to 10	8.1	28	120000	70	6.4	1	RF +
26	1184392	69	M	YES	-	YES	YES	YES	-	-	-	LOOSE STOOLS	-	24	-	-	+	-	-	<8	7	34	146000	78	12.6	1	RF +
27	1131427	59	M	-	-	YES	YES	YES	-	-	YES	-	-	27	-	-	-	-	-	>10	11	36	188000	48	7.6	1	RF +
28	1231937	45	F	YES	-	YES	YES	-	-	-	YES	-	-	30	-	-	+	-	-	8 to 10	9	32	200000	80	7.8	0	RF-
29	1102316	63	M	-	-	YES	YES	-	YES	-	-	-	-	28	-	-	+	-	-	<8	7	40	280000	72	8.8	1	RF +
30	1131062	50	F	YES	-	YES	-	-	-	-	YES	-	-	22	-	-	+	-	-	<8	7.4	42	201000	66	7.4	1	RF +
31	1139666	75	F	YES	-	-	YES	YES	-	-	-	-	-	26	-	-	-	-	-	>10	11	34	150000	68	2.9	1	RF +
32	1294720	72	F	YES	YES	-	-	YES	YES	-	-	-	-	21	-	-	+	-	-	<8	5.5	19	104000	70	9.5	1	RF +
33	1180003	68	F	-	-	YES	-	-	-	-	YES	-	-	24	-	-	+	-	-	>10	11	41	98000	80	5.4	1	RF +
34	1190613	62	M	YES	-	YES	-	YES	-	-	YES	-	-	23	-	-	-	-	-	>10	13	45	184000	72	44	1	RF +
35	1011237	73	M	-	-	-	YES	YES	YES	-	-	-	-	26	-	-	+	-	-	8 to 10	8.4	32	150000	62	3.1	0	RF-
36	1130561	70	M	YES	-	YES	-	-	-	-	YES	-	-	27	-	-	+	-	-	<8	6.4	38	180000	70	3.2	0	RF-
37	1239035	66	M	YES	-	YES	-	-	-	-	-	-	-	26	-	-	+	-	-	8 to 10	9.6	28	212000	62	7.8	1	RF +
38	1119924	64	M	-	-	YES	-	YES	-	-	-	-	-	26	-	-	-	-	-	8 to 10	10	36	242000	60	7.4	0	RF-
39	943495	60	M	-	-	YES	-	-	YES	-	-	-	-	31	-	-	+	-	-	8 to 10	8.1	36	198000	68	9.8	1	RF +
40	1298960	58	F	YES	-	YES	-	-	-	-	YES	RNING MICTURIT	-	27	-	-	-	-	-	8 to 10	9	38	210000	62	9.6	1	RF +
41	1063131	70	M	YES	-	YES	-	YES	-	-	-	-	-	27	-	-	+	-	-	<8	7.2	26	180000	54	8.4	1	RF +
42	1147509	68	M	-	-	YES	-	YES	YES	-	YES	-	-	27	+	-	+	-	-	8 to 10	9.2	34	200000	88	9	1	RF +
43	1137127	60	F	-	-	YES	YES	YES	YES	-	-	-	-	30	-	-	+	-	-	<8	7	28	188000	52	7.4	1	RF +
44	1264946	66	F	YES	-	YES	-	-	-	-	-	-	-	28	-	-	+	-	-	8 to 10	8.4	36	320000	65	11.2	0	RF-
45	1205287	64	F	-	-	-	YES	-	YES	-	YES	RNING MICTURIT	-	27	-	-	+	-	-	8 to 10	8.8	29	212000	42	9.2	0	RF-
46	1168964	72	M	-	-	YES	YES	YES	YES	-	-	-	-	21	-	-	+	-	-	<8	7.8	28	188000	44	12.5	0	RF-
47	1129660	58	M	YES	YES	-	-	-	-	-	-	-	-	24	-	-	+	-	-	8 to 10	8	32	212000	78	11	1	RF +
48	1144765	64	M	-	-	-	-	YES	-	-	YES	-	-	27	+	-	+	-	-	8 to 10	8	42	200000	88	7.2	1	RF +
49	1191491	64	M	YES	-	YES	-	-	-	-	-	-	-	28	-	-	+	-	-	>10	11	44	250000	120	6.4	0	RF-
50	1026059	67	M	-	-	-	-	YES	-	-	YES	-	-	27	-	-	+	-	-	8 to 10	8.4	27	178000	62	8.6	1	RF +
51	1223293	60	F	YES	-	YES	-	-	YES	-	-	RNING MICTURIT	-	28	-	-	+	-	-	>10	12	32	218000	74	6.6	1	RF +
52	1162343	68	M	-	-	YES	YES	-	-	-	YES	-	-	22	-	-	-	-	-	<8	7.8	45	198000	108	11.8	0	RF-
53	1295782	54	F	-	-	YES	-	YES	-	-	-	-	-	26	-	-	+	-	-	8 to 10	8.3	28	200000	88	11.2	1	RF +
54	1134503	50	F	YES	-	YES	-	-	-	-	-	-	-	25	-	-	+	-	-	<8	5	26	140000	78	10.6	1	RF +
55	1142519	64	F	-	-	-	-	YES	-	-	-	-	-	29	-	-	+	-	-	<8	7	34	212000	98	5.6	0	RF-
56	1199149	66	M	-	-	YES	YES	-	YES	-	-	-	-	23	-	-	-	-	-	>10	11	38	165000	72	4.5	1	RF +
57	1178554	68	F	YES	YES	-	-	-	YES	-	YES	-	-	24	-	-	+	-	-	8 to 10	8	41	230000	99	8.8	0	RF-
58	1158354	65	M	-	-	YES	-	-	-	-	-	-	-	24	-	-	+	-	-	8 to 10	9	32	350000	88	16.5	1	RF +
59	1239035	74	M	YES	-	-	-	-	-	-	YES	-	-	26	-	-	+	-	-	<8	5	28	550000	92	12	0	RF-
60	1013222	64	F	-	-	YES	YES	YES	-	-	-	-	-	28	-	-	+	-	-	<8	6	33	210000	102	8	1	RF +
61	1262497	62	M	-	-	YES	-	-	-	-	-	-	-	22	-	-	+	-	-	8 to 10	9	24	140000	144	6	0	RF-
62	1179119	56	M	YES	-	-	-	YES	-	-	YES	-	-	26	-	-	-	-	-	8 to 10	8	29	110000	64	4.5	1	RF +

Sr. No	Mrd No	INVESTIGATIONS																	
		Blood Urea	S.Creatinine	Comorbidity	S.Bilirubin	SGOT	SGPT	Alkaline Phosphatase	S.Phosphate	CORRECTED CALCIUM	Serum Albumin	GLOBULIN	A/G RATIO	Serum Total Protein	Serum LDH	Blood Sugar	Serum Protein Electrophoresis	Serum Immunofixation [if indicated]	Serum Free Light Chain Assay [if indicated]
1	1031945	72	2.7	-	0.54	30	21	54	5.96	12.3	3.39	-8.91	-1.38	9.2	185	247	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
2	1184245	130	5.3	HTN, DM2	0.42	46	11	82	4.91	15.2	3.32	-11.88	-1.28	8.6	640	134	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
3	1183832	120	7.7	DM2	0.7	52	50	46	4.9	13.6	2.6	-11	-1.24	8.9	434	126	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
4	1018698	36	0.8	-	0.1	64	100	88	3.6	11.2	2.7	-8.5	-1.32	9.2	456	112	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
5	1101912	89	9.8	DM2	0.5	90	74	68	7.2	10.5	3.15	-7.35	-1.43	7.8	338	97	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
6	978408	36	1.3	-	0.2	56	60	88	4.05	12.8	3.6	-9.2	-1.39	8.4	160	140	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
7	1133901	43	1.33	-	0.45	60	62	48	4.1	11.8	3.6	-8.2	-1.44	7.8	246	130	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
8	1139420	68	2.8	DM2	1.8	67	60	72	3.6	13.4	3.6	-9.8	-1.37	8.5	826	90	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L - 0.51, FREE K - 74,7, FREE L - 147
9	1135109	109	2.67	HTN	0.2	60	49	60	4.2	13.6	2.03	-11.57	-1.18	8.5	549	98	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
10	1001216	58	1.71	-	0.2	16	27	88	2.6	10.8	3.76	-7.04	-1.53	6.1	340	110	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L- 2.36, K 45.9, L - 19.4
11	1060931	68	3.47	DM2	0.08	25	13	68	3.2	10.2	3.2	-7	-1.46	6.1	124	102	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
12	1080830	61	0.6	-	0.11	23	42	258	4.1	11.2	3.71	-7.49	-1.50	9.2	117	120	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	K/L -1704, K- 186, L- 1.07
13	363606	84	5.07	HTN	0.34	40	20	68	3.9	11.8	3.56	-8.24	-1.43	8.1	200	109	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	K/L - 2.59, K- 13189, L- 5.59
14	1033593	85	4.6	HTN	0.2	78	15	86	4.6	12.8	1.89	-10.91	-1.17	8.2	468	163	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
15	782448	29	1.84	-	0.5	15	18	82	4.9	12.8	1.8	-11	-1.16	7.8	210	110	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L - 10.49, K - 132, L -12.6
16	1024015	99	3.79	HTN	0.25	40	20	86	4.4	10.8	3.61	-7.19	-1.50	7.3	180	102	M SPIKE -	IgA KAPPA MONOCLONAL GAMMOPATHY	-
17	1087788	49	2.2	-	0.2	40	20	66	4.2	14.8	2.28	-12.52	-1.18	8.1	680	120	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
18	1087788	59	2.21	-	0.5	40	52	74	3.83	16.8	3.69	-13.11	-1.28	5.5	256	126	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L- 0.11, K- 31.07, L- 277.35
19	1017605	88	2.6	-	0.1	50	20	356	1.4	10.9	2.8	-8.1	-1.35	6	640	90	M SPIKE -	IgA KAPPA MONOCLONAL GAMMOPATHY	-
20	1263040	115	3.88	DM2	0.29	24	20	98	5.6	10.5	3.58	-6.92	-1.52	5.6	208	120	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L - 0.0002, K - 5.28, L - 22745
21	1185496	37	1.1	-	0.8	40	50	58	4.8	10.8	2.88	-7.92	-1.36	5.2	550	120	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	K/L - 161, K- 279, L-1.73
22	1183712	80	2.94	HTN	0.2	20	18	450	3.2	13	3.1	-9.9	-1.31	6.2	160	98	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L -.002, K-12, L- 5046
23	1271610	48	1.56	-	0.4	68	186	70	1.8	10.4	2.6	-7.8	-1.33	4.9	610	148	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	K/L -288.7, K-2370, L-8.21
24	975155	60	3.3	-	0.4	44	136	240	3.2	11.4	3.6	-7.8	-1.46	6.8	444	98	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
25	1218881	65	2.83	-	0.6	40	42	88	4.7	13.8	3.66	-10.14	-1.36	4.9	165	88	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
26	1184392	46	4.83	DM2	0.9	70	60	46	7.2	14.3	2.6	-11.7	-1.22	5.2	530	110	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
27	1131427	67	3.1	DM2, HTN	0.1	40	20	56	4.7	12.6	2.1	-10.5	-1.20	5.8	720	120	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	K/L - 200, K- 280, L - 1,4
28	1231937	74	2.3	-	0.6	41	40	48	5.2	12.6	2.8	-9.8	-1.29	7.8	600	116	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
29	1102316	72	2.9	CAD	0.5	60	62	68	4.8	12.8	2.6	-10.2	-1.25	5.6	520	110	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
30	1131062	67	3.1	-	0.8	40	60	52	5.1	11.8	2.5	-9.3	-1.27	7.4	580	118	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
31	1139666	93	1.3	-	0.21	18	16	98	4.8	11.2	3.54	-7.66	-1.46	7.2	156	140	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
32	1294720	76	3.07	DM2	2.1	40	22	62	7.4	13.6	2.6	-11	-1.24	5.4	510	120	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
33	1180003	23	1.77	-	0.5	22	38	80	6.2	14.4	3.1	-11.3	-1.27	6.8	488	116	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
34	1190613	24	0.9	-	0.3	40	60	84	4.2	11.9	2.7	-9.2	-1.29	7.8	402	108	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
35	1011237	28	2.7	-	0.2	46	32	320	7.6	12.6	3.7	-8.9	-1.42	9.3	380	102	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
36	1130561	62	1.9	-	0.2	28	22	72	7.2	12.4	2.4	-10	-1.24	8.2	480	112	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
37	1239035	72	2.2	-	0.6	60	56	80	6.2	12.6	3.1	-9.5	-1.33	7.8	212	116	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	K/L - 128, K- 245, L -1,9
38	1119924	70	1.1	-	0.2	26	20	72	6.8	14.6	2.1	-12.5	-1.17	8.4	260	136	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
39	943495	88	1.6	-	0.6	56	40	92	7.8	11.6	3.76	-7.84	-1.48	8.8	286	104	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
40	1298960	72	1.33	-	0.8	20	24	388	6.7	12.7	3.46	-9.24	-1.37	8.4	180	124	M SPIKE +	IgA LAMBDA MONOCLONAL GAMMOPATHY	-
41	1063131	62	2.1	-	0.4	28	26	68	6.2	12.8	3.38	-9.42	-1.36	6.4	168	112	M SPIKE -	IgA KAPPA MONOCLONAL GAMMOPATHY	-
42	1147509	68	2.88	DM2	0.1	22	20	78	7.1	11.8	3.74	-8.06	-1.46	8.4	230	124	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
43	1137127	72	2.4	-	0.4	20	24	68	6.2	12.6	2.4	-10.2	-1.24	7.8	721	110	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
44	1264946	47	2.6	HTN	0.2	16	18	98	4.8	12.8	3.62	-9.18	-1.39	6.8	180	162	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
45	1205287	58	1.88	-	0.2	20	22	366	3.4	16.8	3.4	-13.4	-1.25	9.2	210	88	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	K/L - 0.01, K- 2.53, L- 240
46	1168964	70	2.2	-	0.6	44	38	68	5.2	11.9	2.9	-9	-1.32	8.6	812	110	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
47	1129660	110	1.9	-	0.2	80	60	92	4.4	13.8	3.1	-10.7	-1.29	8.6	510	167	M SPIKE +	IgA KAPPA MONOCLONAL GAMMOPATHY	-
48	1144765	88	4.2	HTN	0.4	34	20	96	3.8	11.2	2.4	-8.8	-1.27	7.8	512	112	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
49	1191491	94	1.4	-	0.6	18	22	88	5.1	10.8	3.56	-7.24	-1.49	9.6	106	88	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
50	1026059	60	1.3	-	0.2	70	62	74	6.1	13.2	3.62	-9.58	-1.38	6.8	168	154	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
51	1223293	78	3.4	DM2	0.1	70	60	76	5.6	11.8	3.52	-8.28	-1.43	7.4	382	110	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
52	1162343	98	2.6	-	0.4	60	34	280	6.4	12.8	1.9	-10.9	-1.17	7.8	388	124	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
53	1295782	88	6.4	DM2	0.6	20	24	78	5.4	14.6	3.64	-10.96	-1.33	9.4	212	88	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
54	1134503	78	4.2	-	0.2	34	42	88	4.2	11.8	1.8	-10	-1.18	9.1	566	98	M SPIKE +	IgG KAPPA MONOCLONAL GAMMOPATHY	-
55	1142519	112	2.8	-	1.3	56	42	82	4.4	13.8	2.2	-11.6	-1.19	7.2	668	102	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
56	1199149	98	1.9	-	1.1	88	64	78	6.2	11.2	3.2	-8	-1.40	8.7	430	124	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
57	1178554	89	7.8	DM2	0.1	76	46	88	5.6	12.7	2.1	-10.6	-1.20	7.6	685	202	M SPIKE -	NORMAL	-
58	1158354	66	3.2	HTN	0.2	20	24	66	4.2	13.2	3.55	-9.65	-1.37	6.8	172	90	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
59	1239035	78	1.8	CAD	0.6	76	88	75	4.8	12.6	2.8	-9.8	-1.29	7.4	524	110	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
60	1013222	43	2.9	-	0.7	46	28	89	3.6	12.8	2.6	-10.2	-1.25	8.1	444	124	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
61	1262497	54	4.2	DM2	0.2	32	12	98	5.2	11.8	3.71	-8.09	-1.46	7.6	230	80	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-
62	1179119	68	3.6	HTN	0.1	66	48	96	4.8	14.2	3.2	-11	-1.29	9.4	620	76	M SPIKE +	IgG LAMBDA MONOCLONAL GAMMOPATHY	-

						Molecular Profile					Outcome					
Sr. No	Mrd No	Bone Marrow Aspirate / Biopsy	Skeletal Survey/ PET-CT Scan	Viral markers [if indicated]	Beta 2 microglobulin [if indicated]	t [4:14]	t [11:14]	t [14:16]	p53 del [17p13 del]	Satge	INDOOR	Treatment Started	OUTDOOR	Treatment Started	Death	Discharge
1	1031945	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	2.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
2	1184245	PLASMA CELL DYSCRASIA	NORMAL	NR	26.4	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
3	1183832	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	18.2	-	-	+	-	Stage III	-	-	YES	YES	-	Yes
4	1018698	PLASMA CELL DYSCRASIA	D8-9 COLLAPSE	NR	6.4	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
5	1101912	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	8.2	-	-	+	-	Stage III	YES	YES	-	-	-	Yes
6	978408	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	3.8	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
7	1133901	PLASMA CELL DYSCRASIA	D4-D6 WEDGE COLLAPSE	NR	4.8	-	-	-	-	Stage II	YES	YES	-	-	Yes	-
8	1139420	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	7.4	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
9	1135109	PLASMA CELL DYSCRASIA	DIFFUSE OSTEOPENIA	NR	14.8	-	-	-	+	Stage III	YES	YES	-	-	-	Yes
10	1001216	PLASMA CELL DYSCRASIA	PARTIAL COLLAPSE D3, D8-10	NR	1.4	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
11	1060931	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	4.9	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
12	1080830	PLASMA CELL DYSCRASIA	# L2 VERTEBRA	NR	1.9	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
13	363606	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	4.5	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
14	1033593	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	14.5	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
15	782448	PLASMA CELL DYSCRASIA	FUSE VERTEBRAL MYELOMA LESI	NR	4.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
16	1024015	PLASMA CELL PROMINENCE	NORMAL	NR	2.5	-	-	-	-	Stage II	-	-	YES	YES	-	Yes
17	1087788	PLASMA CELL DYSCRASIA	LESIONS IN DORSOLUMBAR VERT	NR	5.8	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
18	1087788	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	1.8	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
19	1017605	PLASMA CELL DYSCRASIA	D8 # AND D8-D10 COLLAPSE	NR	5.84	-	+	-	-	Stage III	YES	YES	-	-	Yes	-
20	1263040	PLASMA CELL DYSCRASIA	NORMAL	NR	2.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
21	1185496	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	7.2	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
22	1183712	PLASMA CELL DYSCRASIA	# L2-L3 VERTEBRAE	NR	3.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
23	1271610	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	8.3	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
24	975155	PLASMA CELL DYSCRASIA	# L4 VERTEBRAE	NR	7.6	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
25	1218881	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	2.8	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
26	1184392	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	18.4	-	-	+	-	Stage III	YES	YES	-	-	-	Yes
27	1131427	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	8.8	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
28	1231937	PLASMA CELL DYSCRASIA	DIFFUSE OSTEOPENIA	NR	12.8	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
29	1102316	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	24.6	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
30	1131062	NORMAL	BONY LYTIC LESION	NR	7.8	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
31	1139666	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	5.4	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
32	1294720	PLASMA CELL DYSCRASIA	DIFFUSE OSTEOPENIA	NR	7.6	-	-	+	-	Stage III	-	-	YES	YES	-	Yes
33	1180003	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	13.2	-	-	+	-	Stage III	YES	YES	-	-	-	Yes
34	1190613	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	12.2	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
35	1011237	PLASMA CELL DYSCRASIA	# RIBS LEFT SIDE	NR	3.7	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
36	1130561	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	7.8	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
37	1239035	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	3.2	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
38	1119924	PLASMA CELL DYSCRASIA	DIFFUSE OSTEOPENIA	NR	8.1	-	-	+	-	Stage III	YES	YES	-	-	-	Yes
39	943495	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	1.8	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
40	1298960	PLASMA CELL DYSCRASIA	# L4 -L5 VERTEBRAE	NR	2.4	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
41	1063131	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	3.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
42	1147509	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	2.8	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
43	1137127	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	6.8	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
44	1264946	PLASMA CELL DYSCRASIA	DIFFUSE OSTEOPENIAS	NR	3.7	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
45	1205287	PLASMA CELL DYSCRASIA	# LEFT ANT RIBS	NR	4.2	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
46	1168964	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	7.4	-	-	-	-	Stage III	YES	YES	-	-	-	Yes
47	1129660	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	13.2	-	-	-	+	Stage III	YES	YES	-	-	-	Yes
48	1144765	PLASMA CELL DYSCRASIA	NORMAL	NR	8.6	-	-	+	-	Stage III	-	-	YES	YES	-	Yes
49	1191491	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	2.4	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
50	1026059	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	4.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
51	1223293	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	3.6	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
52	1162343	PLASMA CELL DYSCRASIA	# VERTEBRAE L3-L4	NR	7.2	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
53	1295782	NORMAL	BONY LYTIC LESION	NR	4.2	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
54	1134503	PLASMA CELL DYSCRASIA	NORMAL	NR	6.8	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
55	1142519	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	7.8	-	-	-	+	Stage III	YES	YES	-	-	Yes	-
56	1199149	NORMAL	DIFFUSE OSTEOPENIA	NR	14.8	+	-	-	-	Stage III	YES	YES	-	-	-	Yes
57	1178554	PLASMA CELL DYSCRASIA	NORMAL	NR	5.6	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
58	1158354	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	4.2	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
59	1239035	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	5.6	-	+	-	-	Stage III	-	-	YES	YES	-	Yes
60	1013222	PLASMA CELL DYSCRASIA	BONY LYTIC LESION	NR	8.8	-	+	-	-	Stage III	YES	YES	-	-	-	Yes
61	1262497	PLASMA CELL DYSCRASIA	NORMAL	NR	2.1	-	-	-	-	Stage II	YES	YES	-	-	-	Yes
62	1179119	PLASMA CELL DYSCRASIA	DIFFUSE OSTEOPENIA	NR	8.4	+	-	-	-	Stage III	-	-	YES	YES	-	Yes

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The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Akshay Mehta**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study the clinical profile in newly diagnosed cases of multiple myeloma.

upervisor
Dr. Harmeet Pal Singh
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Assoc. Prof.,
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Co-Supervisor

Dr. Dinesh Gupta
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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

37. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
38. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH 2021

DR AKSHAY MEHTA

DEPARTMENT OF MEDICINE

DAYANAND MEDICAL COLLEGE AND HOSPITAL

LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	To Study the Clinical Profile in Newly Diagnosed Cases Of Multiple Myeloma
For the degree of	Medicine
Name of the candidate	Dr Akshay Mehta
Supervisor	Dr Harmeet Pal Singh Dhooria, Associate Professor, Department of Medicine, DMC&H Ludhiana
Co-supervisor	Dr Dinesh Gupta, Professor & Head, Department of Medicine, DMC&H Ludhiana Dr Davinder Paul, Assistant Professor, Department of Oncology, DMC&H, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Multiple myeloma is a malignant disorder characterized by proliferation of a single clone of plasma cells derived from the beta cells in the bone marrow. Multiple myeloma is a neoplastic plasma cell dyscrasia characterized by a clinical pentad: a) anemia b) monoclonal protein in serum or urine, or both, c) abnormal bone radiographs and bone pain; d) hypercalcaemia and e) renal insufficiency or failure.

Aim of Study: 1. To study the clinical profile in newly diagnosed cases of multiple myeloma. 2. To assess the molecular profile in newly diagnosed cases of multiple myeloma.

Materials & methods: The study will be conducted in the Department of Medicine, Department of Oncology and the Allied Specialties of Medicine of DMCH, Ludhiana

- Inclusion Criterion -
  1. Newly diagnosed cases of multiple myeloma [inpatients and outpatients] 2. The patients who agree to give the consent for the study
- Exclusion Criterion –
  1. k/c/o multiple myeloma on follow up. 2. Patients who do not give the consent for the study. 3. Monoclonal Gammopathies of undetermined significance[MGUS]. 4. Plasma cell leukemias
- Duration of Study/ Number of Cases- Time bound study -1year [March 2021- February 2022]

Clinical Significance:

This study will help us know the clinical profile, molecular profile, and stage of the disease at the time of diagnosis in the patients of mutiple myeloma presenting to a tertiary care hospital.

KEYWORDS: Multiple myeloma, anemia, hypercalcemia, renal failure, bone lesions, molecular profile.

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA"** exist in the Department of General Surgery, DMC&H, Ludhiana and will be provided to be candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate himself under our supervision and guidance.

Supervisor

Dr Harmeet Pal Singh Dhooria
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Department of Medicine
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Co-Supervisor(s)

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HEAD OF DEPARTMENT

Dr. Dinesh Gupta
Professor and Head
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Place: _____

Date: _____

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Akshay Mehta
Department	Medicine
Topic of Thesis	TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA
Likely date of appearing in PG examination	MAY 2023
Date of enrollment	26th July 2020
Name of Head of Department	Dr. Dinesh Gupta
1) Supervisor **2) Co-Supervisor**	Dr. Harmeet Pal Singh Dhooria Dr. Dinesh Gupta Dr. Davinder Paul
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Akshay Mehta H.NO 243, B Block , Sirsa, Haryana
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Medicine
4	DATE OF ADMISSION OF COURSE	26th JULY 2020
5	TITLE OF THE TOPIC	To study the clinical profile in newly diagnosed cases of Multiple Myeloma.

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Multiple myeloma is a malignant disorder characterized by proliferation of a single clone of plasma cells derived from the beta cells in the bone marrow. It is the second most common adult hematological malignancy and it is the most common cancer with skeletal components as its primary site. Multiple myeloma is a neoplastic plasma cell dyscrasia characterized by a clinical pentad:

a) anemia b) monoclonal protein in serum or urine, or both, c) abnormal bone radiographs and bone pain; d) hypercalcaemia and e) renal insufficiency or failure.

With the exception of monoclonal gammopathy of undetermined significance; it is the most common plasma cell dyscrasia, with an incidence of approximately 4.5/100,000 per year in the United States.

Incidence increases with age [median age of diagnosis is around 69 yrs], is almost equal in males and in females and higher among blacks than in whites. [1]

The exact cause of multiple myeloma is unknown. Increased incidence has been reported in people exposed to radiation [2], petroleum, rubber, wood and plaster products, cosmetologists and farmers. Viruses may also be involved in the pathogenesis. Genetic aberrations have been noted in 20-60% patients with t(11:14) being the most frequent translocation. Among the losses, monosomy or partial deletion of chromosome 13 is the most common finding [3].A variety of chromosomal alterations have been found in patients with myeloma: hyperdiploidy, 13q14 deletions, translocations t [11:14], t [14:16], t [4:14], 1q amplification or 1 p deletion, deletion 17p13. However no single common molecular pathogenetic pathway has yet emerged. Molecular Profile includes the myeloma panel workup which will include the translocations -t[11:14], t[14:16], t[4:14],and deletion - del 17p13 [p53].

Cytokines play an important role in the proliferation of myeloma cells. The growth and differentiation of myeloma cells is supported by interleukin-6.

The clinical manifestations are due to the infiltration by plasma cells and secretion of the monoclonal protein M by them. Replacement of the morrow by plasma cells and renal damage produces anemia which may present as pallor, fatigue etc. A hemoglobin concentration of less than 120 g/l occurs in 40-73% of patients at presentation and contributes to weakness and fatigue in as much as 82% of patients. The anemia is normochromic, normocytic in most patients. Bone pain is the predominant symptom in 80% patients. An increase in osteoclastic bone resorption in myeloma is usually associated with a marked impairment in bone formation. Approximately 75% of patients have punched out lytic lesions, osteoporosis or fractures on conventional radiography [4].Nerve root compression may occur due to vertebral collapse. Hypercalcaemia occurs in 18-30% patients as a result of bone destruction. Approximately 13% has concentrations greater than 11mg/dL. The hypercalcaemic patient may complain of fatigue, constipation, nausea or confusion.

Patients of multiple myeloma are at risk for developing recurrent infections due to deficiency in antibody production; abnormal cell mediated immunity, and in advanced cases, neutropenia. Approximately 25% of myeloma patients have a serum creatinine value greater than 2 mg/dL at diagnosis [5].Various factors may contribute to renal failure, including cast nephropathy, hypercalcaemia, dehydration, hyperuricaemia and the use of nephrotoxic drugs. A hyperviscosity syndrome may occur leading to headaches and visual disturbances.

The spectrum of neurological complications in multiple myeloma ranges from direct compression, radiculopathy, spinal cord compression, peripheral neuropathy, slowed mentation from hyperviscosity, hypercalcaemia or uraemia, autoimmune or cytokine mediated (peripheral neuropathy).Rarely, POEMS syndrome[6] [polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes] observed in osteosclerotic myeloma with prominent sensory neuropathy.

6.2 REVIEW OF LITERATURE

Samuel Solly reported the first well documented case of myeloma in Sarah Newbury in 1844 (mollities ossium) [7]

Several years later, William Mac intyre described and recorded, from a case in Thomas Alexander Mc Bean, the properties of the disease now called multiple myeloma. Mac intyre and Dalrymple described the post mortem examination of Mc Bean's bones: the former described the affected bones as softened and fragile, with their interiors replaced with a soft "gelatin form" blood red substance.[8]

The term multiple myeloma was coined in 1873 by Von Rustizky who independently described a similar patient to emphasize the multiple bone tumors that were present.

Mac Intyre and Bence Jones noted and described some of the peculiar urine properties of the patient Mc Bean. On heating, the urine was found to abound in animal matter which dissolved on addition of nitric acid, but reappeared on cooling these urinary proteins became known as Bence Jones proteins. [9]

Serum electrophoresis, described by Tiselius in 1937 made it possible to separate serum proteins.

Kunkel hypothesized that the monoclonal proteins were the product of malignant plasma cells and were the equivalent of normal antibodies product by normal plasma cells.

Salmon and Smith and Durie and Salmon [10] developed methods to quantitate the total body burden of tumor cells and stage patients in 1970 and 1975 respectively.

Robert A. Kyle et al[6] in Mayo Clinics Proceedings 2003 published a review of 1027 patients of newly diagnosed Multiple myeloma and reported bone pain as the most common presentation seen in 58% patients followed by fatigue in 32% patients. The median haemoglobin reported was 9.9g/dL in patients with fatigue and 11.lg/dL in patients without fatigue. Weight loss was reported as the presenting feature in 24% patients, paraesthesias in 5% and fever in 0.7% cases.

Riccardi A. Et al[11] in European Journal Of Cancer compared the presenting features of 3 series of patients of Multiple Myeloma and reported decreasing incidence of bone pain, hypercalcemia, neurological symptoms and hyperviscosity over the years from 90% between 1960 and 1971, 86% between 1972 and 1986 and 66% between 1987 and 1990. The percentage of asymptomatic patients diagnosed by chance increased from 14% to 34%. The incidence of bone pain decreased from 68% to 37%, incidence of systemic symptoms like weakness, infections, fever and weight loss have increased in incidence.

Mai Yu-jie et al[12] in a study of 532 patients reported anemia in 93.5% patients, fatigue in 66.9%, bone pain in 53.7%, bleeding in 23.4%, fever in 20%, solitary mass in 8%, blurred vision, rash or edema in 10.4% patients.

Ruiz-Arguelles et al [13] studied 66 cases of Multiple Myeloma and found fatigue in 66% cases, bone pain in 54%, weight loss in 47%, anemia 75% in females and 96% in males. Four cases of non secretory myeloma were reported.

Wang GM [14] studied 25 cases of Multiple Myeloma and found bone pain followed by anemia as the most common presenting feature.

Kelly E. Dooley [15] reviewed cases of newly diagnosed Multiple myeloma and reported clinical polyneuropathies in 13% and electrophysiological evidence of neuropathy in 39%.

Marino Clavio et al [16] in 1996 compared the clinical features in patients of Multiple Myeloma between 65 years to 75 years of age and those above 75 years. Presenting features did not differ significantly in patients in either group. Lesser number of patients with renal failure was found in patients above 65 years of age as compared to overall incidence.

Fentress et al [17] studies large series of patients of Multiple Myeloma and found bone abnormalities in conventional radiographs in 79% cases, lytic lesions in 67% cases, osteoporosis in 23%, pathological fractures 26%, compression fractures in 22% and no bone abnormalities in 21% cases.

R. Kapoor et al [18] studied 150 patients of Multiple Myeloma. Only 5 patients were younger than 30 years. No patient younger than 30 years had anemia or hypercalcemia. All patients had bone pain and lytic bone lesions and 3 patients had extramedullary involvement.

Walsh [19] found clinical evidence of neuropathy in 13% patients in a prospective study and electrophysiological evidence in 30% cases.

Gunnar Birgegard [20] et al studied 704 patients and incidence of anemia at the time of enrolment was 72.9%.

Molloy et al [21] presented a case report of a patient presenting with carpal tunnel syndrome, erosive arthritis and invasive tumoral arthritis as the initial clinical presentation of Multiple Myeloma.

Edgardo et al [22] studied a large number of patients of newly diagnosed Multiple Myeloma and found fatigue and bone pain predominantly in back or ribs with or without pathological fractures as the most common presentation of Multiple Myeloma. In their study 15-30% has hypercalcemia with concomitant renal failure and 10% presented with other symptoms like hyperviscosity, spinal cord compression, radicular pain, soft tissue deposits or bleeding.

Baykul et al [23] reported a case with an unusual combination of oral complaints (mandibular and maxillary destruction) as the initial feature of Multiple Myeloma.

Dispenzieri et al [24] described neurological manifestations with compression of spinal cord or nerve roots in 5% cases with thoracic region of spinal cord involved most commonly.

Neta Goldschmidt [25] in his study revealed that of the 110 patients, 96 (87%) had at least 1 pain complaint in the 2 years before the diagnosis of MM. Back and musculoskeletal pain were more common than other complaints, with a mean number of clinic visits of 3 and 2.6, respectively, for these. More than half of the patients had at least 1 infectious episode in the 2 years before the diagnosis of MM. Weight loss and fatigue were present in 9% and 25%, respectively. He included all other relevant complaints, including peripheral edema,

constipation, presyncope, syncope, and dizziness, in 1 group named “Others.” These “other” complaints were found in 33% of patient.

QIAN et al [26] study revealed two most common complaints were bone pain (51.2%) and fatigue (48.0%). Anemia (Hb≤100 g/L in female, Hb≤ 110 g/L in male) was present initially in 69.4% patients.

In all the studies reviewed, it was seen that bone pain was the most common presenting feature of Multiple Myeloma followed by anemia, renal involvement and hypercalcemia.

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study the clinical profile in newly diagnosed multiple myeloma patients.
2. To study the molecular profile in newly diagnosed cases of Multiple Myeloma.

7.0 MATERIALS AND METHODS

7.1 SOURCE OF DATA

The study will be conducted in the Department of Medicine, Department of Oncology and the Allied Specialties of Medicine of DMCH, Ludhiana.

7.2 METHOD OF COLLECTION OF DATA

Inclusion Criterion:

1. Newly diagnosed cases of multiple myeloma [inpatients and outpatients].
2. The patients who give the consent for the study.

Exclusion Criterion:

1. k/c/o multiple myeloma on follow up.
2. Patients who do not give the consent for the study.
3. Monoclonal Gammopathies of undetermined significance [MGUS].
4. Plasma cell leukemias.

1. The patients who will be newly diagnosed with Multiple Myeloma on the basis of revised IMWG diagnostic criteria 2014 will be enrolled for the study.
2. A prospective observational study will be performed on all the patients.
3. Patients will receive the explanation of the nature of the study and a written consent will be taken.
4. Information will be collected through a predesigned performa for each patient enrolled into the study.
5. Detailed history and examination will be done.
6. Laboratory parameters to be evaluated will be collected from patient's medical records.
7. Molecular workup done in the newly diagnosed cases will be collected from patient's records**.**

Panel: Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and smouldering multiple myeloma

Definition of multiple myeloma

Clonal bone marrow plasma cells ≥10% or biopsy-proven bony or extramedullary plasmacytoma and

Any one or more of the following myeloma defining events [MDEs]:

1. Evidence of end organ damage [CRAB lesions] that can be attributed to the underlying plasma cell proliferative disorder, specifically:

- Hypercalcemia: serum calcium >0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (> 11 mg/dL)
- Renal insufficiency: creatinine clearance <40 mL/min or serum creatinine >177 mmol/L (> 2 mg/dL)
- Anemia: hemoglobin value of >2 g/dL below the lower limit of normal, or a hemoglobin value < 10 g/dL
- Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT

2. Any one or more of the following biomarkers of malignancy (MDEs):

- Clonal bone marrow plasma cell percentage >60%
- Involved: uninvolved serum FLC ratio ≥100 (involved FLC level must be atleast 100 mg/L).
- >1 focal lesion on MRI studies (at least 5 mm in size)

Definition of smouldering multiple myeloma

Both criteria must be met:

• Serum monoclonal protein (IgG or IgA) ≥30 g/L or urinary monoclonal protein ≥500 mg per 24 h and/or clonal bone marrow plasma cells 10–60%

• Absence of myeloma defining events or amyloidosis

Revised International Staging System

STAGE I

- Serum albumin >3.5 g/dL
- Serum B2-microglobulin < 3.5 mg/L
- No high-risk cytogenetic features
- Normal serum lactate dehydrogenase level

STAGE II

Neither stage I nor stage lll

STAGE III

- Serum B2-microglobulin ≥ 5.5 mg/L
- AND one of the following:

  (a) High-risk cytogenetic features :

  t(4:14)

  t(14;16)

  del(17p)

  (b) Elevated serum lactate dehydrogenase level

The clinical heterogeneity of Multiple Myeloma is dictated by the cytogenetic aberrations present in the clonal plasma cells (PCs). Cytogenetic studies in MM are hampered by the hypo proliferative nature of plasma cells in MM. Therefore, fluorescence in situ hybridization (FISH) analysis is an attractive alternative for evaluation of numerical and structural chromosomal changes in MM.

In contrast to conventional cytogenetic, interphase fluorescence in situ hybridization (FISH) can detect cytogenetic abnormalities independent of cell proliferation. As such, the sensitivity of FISH is higher than conventional cytogenetic.

Heparinised bone marrow blood sample is taken and Plasma cells are counted from bone marrow smears and fluorescence-in-situ hybridization (FISH) is performed using various probes as described below for each of the genetic abnormality. Number of cells analyzed per probe – 100 cells.

1. Zytolight SPEC Orange TP53/ CEN 17 SPEC Green DC DNA probe [for p53 deletion]

2. Zytolight SPEC FGFR3/ IGH Dual Colour Dual Fusion Probe [for t(4;14)]
3. Zytolight SPEC CCND1/ IGH Dual Colour – Dual Fusion Probe [for t(11;14)]
4. Zytolight SPEC MAF / IGH Dual Colour – Dual Fusion Probe [for t(14;16)]

Duration of Study: All the patients of newly diagnosed MM during 1 year period [March 2021-February 2022] will be enrolled for the study.

Outcome:

Indoor – Discharged /DAMA/ Death

Treatment started – Yes / No

Outdoor – Treatment started – Yes / No

Statistical Analysis:

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes

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PROFORMA

Sr No.

Name

Mrd No.

Age/ Sex:

Father's Name

Address

Occupation

Date of Admission

Date of Discharge

Presenting Complaints And Duration

- Bony Pains
- Fractures
- Fatigue
- Dyspnea
- Weight Loss/Loss Of Appetite
- Decreased Urine Output
- Altered Sensorium
- Fever
- Any Other Complaints

Date of Diagnosis

Comorbid Illness

Signature of Candidate

Signature of Supervisor

EXAMINATION

GENERAL EXAMINATION

ECOG PS

BMI

Pulse Rate
Blood Pressure
Respiratory Rate
Cyanosis

Clubbing
Icterus
Pallor
JVP

SYSTEMIC EXAMINATION

1. Respiratory System

2. Abdomen

3. Cardiovascular System

4. Central Nervous System

Signature of Candidate **Signature of Supervisor**

INVESTIGATIONS

HB

PCV

Platelet count

ESR

TLC

DLC

PBF

Blood Urea

S.Creatinine

S.Bilirubin

SGOT/SGPT

Alkaline Phosphatase

S.Phosphate

Corrected Calcium

Serum Albumin

Serum Total Protein

Serum LDH

Blood Sugar

Serum Protein Electrophoresis

Serum Immunofixation [if indicated]

Serum Free Light Chain Assay [if indicated]

Signature of Candidate **Signature of Supervisor**

Bone Marrow Aspirate / Biopsy

Skeletal Survey/ PET-CT Scan

Viral markers [if indicated]

Beta 2 microglobulin [if indicated]

Molecular Profile -

t [4:14]

t [11:14]

t [14:16]

p53 del [17p13 del]

Stage

Final Diagnosis

Outcome –

INDOOR – Discharge / Dama / Death

Treatment Started – Yes / No

OUTDOOR – Treatment Started – Yes / No

Treatment Plan / Given:

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA"**. I am ready to participate in this research work on my free will. I affirm that I have not been given any financial inducement or pressure to accept this. The purpose of this research work has been explained to me and I believe that it is for the benefit of science and humanity. I have been explained about the risk in this research and I think this risk is very rare. I have been explained about the process of participation in this study.

I can withdraw my participation from this research at any time and my withdrawal will have no effect on my treatment.

....
Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है। मुझे इस शोधकार्य में भाग लेने की विधि के बारे में समझाया गया है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____

गवाह के हस्ताक्षर

नाम:

_____

रोगी के हस्ताक्षर/अंगूठे का निशान

नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"TO STUDY THE CLINICAL PROFILE IN NEWLY DIAGNOSED CASES OF MULTIPLE MYELOMA" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ